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JUN 13 1933

l. 40. No. 3. (New Series. Published Bi-Monthly). May, 1933
ablished 1902.

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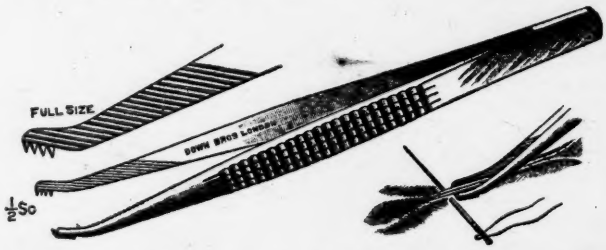

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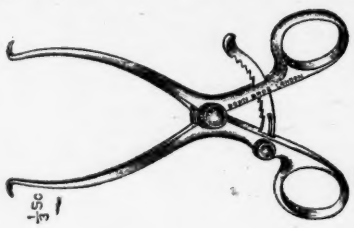

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The Journal of
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VOL. 40, No. 3 NEW SERIES MAY, 1933

On the Physiology and Pathology of the Isthmus Uteri.

BY

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PART I.

PHASIC PICTURE OF THE ISTHMUS.

THE existence of an isthmus uteri, the necessity of a threefold division of the uterus into the corpus, the isthmus and the cervix seems, in spite of considerable literature extant on the subject, not to be commonly accepted by all those who concern themselves with the anatomy, physiology and pathology of the womb.

What is to be understood by the isthmus uteri? Certainly no longer what Langer called the isthmus in his time. He used the word isthmus for what we nowadays call the inner os uteri. We understand by isthmus, not indeed the circular border-line between the cavity of the corpus and the cavity of the cervix but the hollow space in the cranial part of the cervix, the mucous membrane of which resembles that of the corpus, without being identical with it either morphologically or physiologically. The mucous membrane of the isthmus differs fundamentally also from that of the larger caudal segment of the cervix.

That all anatomists do not recognize the isthmus as a distinct section of the uterus appears, for example, from the fact that in Gray's "Anatomy: Descriptive and Applied," published in 1930, the isthmus does not receive any treatment either in illustration or description. The same applies to the Atlas of Toldt-Hoch-

stetter. In his "Lehrbuch der Systematischen Anatomie," which appeared in 1923, Tandler speaks only of the corpus and cervix, and of the boundary between the two, the inner os uteri. Yet the same author devotes a separate detailed section to the isthmus in his treatment of anatomy in Stoeckel's "Handbuch." In Testut and Jacob's "Traité d'Anatomie Topographique," 1931, the isthmus is indeed illustrated but insufficiently described.

The necessity for the threefold division of the uterus was advocated by Veit and later on by Aschoff in particular. The whole question came very much to the fore because of interest in the lower uterine segment of the pregnant womb, and its relations to the isthmus of the non-pregnant organ. Besides Veit and Aschoff, Rosthorn, Heger, Stieve, Hartmann, Ogata, Sternberg, Stromeier, Moritz and Nürnberger have advocated the existence of the isthmus and the recognition of it as an independent part of the womb. Bayer completely denied the existence of the isthmus in the non-pregnant womb. Büttner grants the mucous membrane of the isthmus certain morphological differences, but denies functional differences. Gräsel goes further still and considers the morphological difference also as inessential. On the other hand Poirier in his "Traité d'Anatomie Humaine," 1925, describes "the three portions of the uterus; the body, the isthmus, the neck." The author justifies this triple division in a remarkable way; "this division of the uterus into three segments is exact not only from the anatomical point of view, but also from the pathological; the lower part of the anatomical neck, that is to say the histological neck, has a quite special pathology, very different from the rest of the uterus." As we shall see this affirmation can be made equally justly of the isthmus. Specially clear descriptions of the isthmus are to be found in the fine work of Stieve on the neck of the womb 1927.

A word requires to be said regarding nomenclature. According to Aschoff the border line between the corpus and the cranial end of the isthmus is denominated the orificium uteri internum anatomicum while the boundary between the caudal end of the isthmus and the cervix is named orificium uteri internum histologicum. The Nomenclature Commission of the Anatomical Society thought it necessary to replace these perfectly good terms with still better ones, and for the orificium uteri internum anatomicum has laid down the name orificium isthmi internum, and for the orificium uteri internum histologicum the name orificium isthmi externum. Whether this alteration of the terms is really an improvement

may well be doubted. Only an opening that leads outwards can be properly termed an os externum. If Aschoff's nomenclature, which is certainly exceedingly serviceable and generally comprehensible, must be absolutely altered, it would be more to the purpose to speak of an orificium isthmi superius sive craniale (proximale) and an orificium isthmi inferius sive caudale (distale). It is my opinion, however, that Aschoff's terminology is entirely useful, but it must not be understood that the orificium isthmi anatomicum coincides to a millimetre with the point of attachment of the peritoneum or the entrance of the arteria uterina. Against this Tandler, Halban, Hegar, Nürnberger, Stieve, and Schröder have already expressed themselves.

According to Stieve the length of the isthmus is about 4.5 mm.; according to Aschoff the limit of the mucous membrane of the cervix lies 8 mm. to 10 mm. deeper than the microscopically flexible orificium uteri internum. According to Schröder the isthmus is the uppermost centimetre of the tubular canal of the uterus. Having investigated a very large quantity of material, I find the length of the isthmus extraordinarily variable, not only in pathological but also in normal uteri. The boundary between the cervical mucous membrane and the corpus-like membrane, which Aschoff terms the orificium internum histologicum, is, according to this author, not quite sharply defined, as cervix— and corpus— glands mingle together over an extent of about one mm.

I have been occupied now for five years with the problem of the isthmus and investigated, macroscopically and microscopically, many hundreds of uteri. It is indeed true that the orificium isthmi superius does not coincide to a hair's breadth with the point of attachment of the peritoneum or the entrance of the arteria uterina. Still, if the uterus is carefully opened and the mucous membrane preserved, the upper and also the lower limit of the isthmus can be distinguished almost without exception even with the naked eye. With regard to the upper limit there exist no difficulties whatever when the mucosa is pre-menstrual or corresponds to the second half of the interval. Then the 2 mm. to 5 mm. thick, some times distinctly thicker, soft mucous membrane at the upper limit of the isthmus breaks off sharply, although in this phase the mucous membrane of the isthmus is occasionally thicker than usual. The boundary line is exceptionally clear when a tubal pregnancy exists or a uterine decidua is present (Ruge, Strassmann, and Schultze). I assert, however and I have set up macroscopical demonstrational

preparations in proof of this—that in the post-menstruum too, the upper limit of the isthmus is almost always clearly perceptible with the naked eye. If all uteri are systematically examined to this end, such expertness is obtained in the macroscopic delimitation of specimens of the uterus that the succeeding microscopical investigation (I should recommend here the use of Tetrander sections throughout) verifies the limits fixed by the naked eye.

Although it is true that the cervical mucous membrane almost always overlies the isthmus glands for a short distance (Stieve, and Schröder), yet even the lower boundary of the isthmus can, with a little practice, be correctly fixed by the naked eye. It manifests itself sometimes as a low fold, sometimes as a shallow furrow. For this also I have macroscopic demonstrational preparations at hand, which I do not reproduce here in order to keep down the number of figures. I am certainly of Nürnberger's opinion that a histological investigation always presents the limits of the isthmus clearly, but I do not hold the view that a microscopic investigation is always necessary. Seitz too notes that the isthmus can be distinguished by the naked eye. That concerns, however, only the functioning uterus. The infantile and senile uterus more frequently show an obliteration of the limits of the isthmus, so that in these cases a microscopic delimitation is necessary.

Several authors (Nürnberger, Tarlo, Schröder, Moritz and others) point out that the glands in the corpus run from internally below to externally above, while those in the isthmus are directed from internally above to externally below. This criterion does not apply to many uteri which I have investigated. Often enough, in the developing phases, the glands in the corpus are arranged not obliquely but vertically to the surface epithelium. In the isthmus, however, I find, on the basis of numerous investigations, sometimes but by no means always, the arrangement of glands from internally above to externally below, which is stated to be typical. Often, the exceedingly short glands are arranged vertically to the surface epithelium, and not infrequently the ducts run quite parallel to the surface epithelium and close underneath it. We have other and more trustworthy histological indications for the delimitations of the uterine isthmus. It is true that regarding these too, acounts at variance with each other are given in the literature on the subject. Aschoff aims at distinguishing the mucous membrane of the isthmus from the mucosa of the corpus in that the former thrusts deeper and more irregular serrations into the musculature. I would point out at once that

this differential indication fails in the majority of cases. Nürnberger declares, quite correctly, that the epithelium of the isthmus is both morphologically and tinctorially identical with that of the corpus. The cells are low, the nucleus is rounded and lies centrally. Mucus is never indicated in the epithelia of the isthmus in stainings for mucus; only outside the cells are there to be found mucicarmine-positive masses. In this the author agrees entirely with Sternberg and Eva Moritz, who (in contrast to Büttner, who considers mucus-staining useless as a means of distinction) hold that tincture with mucicarmine or kresylviolet is diagnostically valuable. I am convinced about the value of mucus-staining, but it is not required in the majority of cases as the ordinary colouring methods render it possible to distinguish between the strongly cylindrical cells of the cervix and the elements of the isthmus. Nürnberger says rightly, besides, that the cells of the cervix when stained with mucicarmine appear entirely of a deep red colour while in the cells of the epithelium of the isthmus and corpus the mucus is present in only a preliminary stage. At this point Sternberg's remark must be noted in which he recommends that the concentrated solution should be diluted tenfold and the sections allowed to lie in it for half an hour.

Almost all authors, with Aschoff at their head, describe the mucous membrane of the isthmus as thin and poor in glands, a statement to which I am able to subscribe. Gräsel, it is true, denies all morphological differences. Moritz characterizes the isthmus with the following qualities:

(1) The relative thinness of the mucous membrane; (2) The greatly diminished number of glands; (3) The characteristic arrangement of the latter. To this must be added the result of mucus-staining.

Stieve finds no glands at all in some cross sections through the isthmus, while in other cases more glands are present. The epithelium is a low cylindrical epithelium. The plasmic body is narrow, dark, frothy with finely granulated stratifications. Ciliar hairs are seldom found. The content of the isthmus glands entirely resemble that of the corpus glands. Cysts are frequently formed in the area of the isthmus, but the content of these cysts is differentiated by their finely granulated structure from the mucous content of the cervical glands. (I would add also from the mucous content of the cysts which proceed from the cervical glands.) With this statement of Stieve I must declare myself to be in entire agreement on all points.

With regard to the stroma there are only incidental remarks.

Schröder says, for instance, that the stroma is relatively close-meshed. Stieve describes the uterus of a 17 years old girl and emphasizes that the basic tissue between the glands is very rich in small, round, and spindle-shaped cells but contains only a few blood-vessels. I should like here to lay emphasis upon a remark of Schröder and Tarlo with regard to alterations in pregnancy of the mucous membrane of the isthmus.

Tarlo stresses that the decidua proceeding from the mucous membrane of the isthmus does not show any pronounced compacta. The spongy tissue is thin and shows a small number of elongated glands. Schröder says that in pregnancy the mucous membrane of the isthmus forms essentially only a spongy tissue. The compacta is comparatively much less than in sections of the corpus or else entirely absent. Here I must also quote the remark of Stieve with regard to the isthmus of a pregnant woman with a small embryo of 39.5 mm. He describes the mucous membrane of the isthmus which is only 0.5 mm. to 1.5 mm. thick, while the decidua is 3 mm. to 4 mm. thick. He finds decidual cells are absent in the isthmus, while they are to be found in quantities and in the finest development in the corpus. He was able to establish the same fact also with regard to other pregnant uteri. His investigation of uteri in the last months of pregnancy causes Stieve to make the very important observation that the decidua in the lower uterine segment permanently differs from that of the remainder of the body of the womb. I consider these observations, the contents of which I can fully confirm, to be very important for the understanding of the mucous membrane of the isthmus, and I shall have to return to them later on.

We shall arrive at complete knowledge of the normal histology of the isthmus only by considering the phases of a particular case. I will, therefore, briefly discuss the appearance of the isthmus in the pre-menstruum, in the interval, and in the post-menstruum. The literature on this subject is not very copious. The best accounts of the pre-menstrual and menstrual mucous membrane of the isthmus are those of Nürnberger and Schröder. The former author truly observes that the swollen mucous membrane of the corpus stops short with an overhanging swelling at the inner os uteri. The transition from the corpus to the isthmus is immediate. In the glands the epithelium is lower than in the corpus. The cells are cylindrical, but not so high as in the glands of the corpus: the nucleus fills the cell fairly completely. The saw-tooth-like shape of the glands is recognizable but not so defined as in the corpus. "The stroma does not show any decidual

alteration." In the upper third of the isthmus can be distinguished a certain differentiation between a surface layer and the basalis. The stroma at the surface is more loosely composed than the stroma of the basalis. Here also there exists an oedematous saturation, the vessels are distended. In the lower two-thirds of the isthmus the differentiation of a surface and a basal layer disappears. In menstruation the surface layer of the compacta is cast off, an infiltration of small cells and a saturation with blood takes place. In the distal portions of the isthmus the surface epithelium is lifted off by the collection of sub-epithelial liquid. It does not go so far as effusions of blood into the stroma. Towards the end of menstruation the surface epithelium, together with the layer of the stroma which borders on it is lacking, but the loss of substance is inconsiderable. There are to be found islands of intact surface epithelium. The isthmus consequently takes part in the menstrual cycle to a very limited extent. In contrast to the corpus, the isthmus manifests a very slight indication of the pre-menstrual alteration which is confined to the uppermost layers of the mucous membrane. The isthmus shares in the menstrual blood-effusion "but the occurrences which take place here do not attain by any means, either in quantity or quality, the same intensity as in the corpus. While in the corpus a complete loss of the functional layer is reached, in the isthmus only the surface epithelium, together with the immediate neighbouring parts of the stroma of the mucous membrane is cast off." Schröder designates the share of the isthmus in the cycle as exceedingly limited, it is true, but still perfectly definite. An actual functionalis is not formed, but only a low mucous membrane remains in existence. "That which runs parallel with the cycle of the corpus is clearly seen in the alteration of the epithelium which corresponds entirely with its secretional character and, further, the form of the short glands may show a distinctly serpentine or saw-like form. The stroma too may also loosen and its cells grow larger. Even a desquamation of the surface epithelium takes place and the raw surface of the endometrium of the corpus extends thereby as far as the edge of the cervical epithelium. In this way a rudimentary pre-gravid reaction is set up and thereby an imperfect preparation for pregnancy for the ovum in the isthmus."

The description which I have given here from the two named authors I am able, on the basis of my investigations, to support unreservedly and wish only to add a few observations. I have set up several uteri showing a pre-menstrual phase for the sake

of macroscopic demonstration in order to show the sudden stop of the thick mucous membrane at the upper edge of the isthmus. In sagittal sections through the uterus this boundary line shows at times as a steep drop, sometimes the pre-gravid mucosa of the corpus shows a roof-like overhang above the uppermost part of the mucous membrane of the isthmus. But sometimes also there is to be observed a gradual inclination of the thick mucous membrane of the corpus towards the thin (although in contrast with the post-menstruum somewhat thicker) mucous membrane of the isthmus (Fig. 1).

The histological picture of the mucous membrane of the isthmus in the pre-menstruum may take various shapes. In spite of a distinct pre-gravid alteration of the mucous membrane of the corpus, the mucous membrane of the isthmus may remain quite thin and uncommonly poor in glands, in which condition the glands may not take on at all the form of a saw or may only suggest it. These are the cases in which the mucous membrane of the corpus drops steeply towards the mucous membrane of the isthmus. In other uteri the mucous membrane of the isthmus shows, not only in its cranial section but throughout its whole length very clear phenomenon of the pre-menstrual phase. The glands are distended, sometimes even more so than in the corpus (Fig. 2). The tendency of the glands of the isthmus to dilatation and formation of cysts is of course known.

But while in the corpus the glands show a regular parallel arrangement and descend almost vertically from the surface epithelium, the direction in which the glands of the isthmus run is quite irregular.

Particularly decisive, however, are the differences in the surface of the mucous membrane; while the mucous membrane of the corpus presents a broad, richly vascularized layer, consisting of loosely fitted, swollen (pre-decidual) elements, within which the neck portions of the glands lie, the corresponding portion in the isthmus is very much thinner, and for the most part never attains development (Fig. 3).

This appears to me to be of considerable importance. While in the pre-menstruum the mucous membrane of the corpus reacts upon the ovarian hormonal stimulation with the formation of a pre-decidual surface layer of stroma, a functionalis and a deep mucous membranial portion with a close-lying, inactive fundus of glands, in the isthmus no such triple division of the mucous membrane is arrived at. In particular, the formation of a "pre-decidual compacta" is lacking or only slightly indicated.

The entirely correct observation of Schröder and Tarlo, quoted quoted above agrees very well that a definite compacta is lacking to the decidua, in so far as it proceeds from the mucous membrane of the isthmus. We know from the study of young ova that human nidation is superficial. The ovum embeds itself among the swollen cells of the stroma, between the excretory ducts of the glands, and there it remains till the end of pregnancy. With human beings the implantation is superficial. Under the ovum there forms the spongiosa which is of such importance for the mechanism of normal separation of the placenta, post-partum. In the pre-gravid stage the superficial layer of stroma cells is loosened, thickened, fertilized with oedematous liquid and enriched with gylcogen and in this way prepared for the ovum. This exceedingly important preparation is absent in the isthmus, whence the absence of any tendency to ovum-implantation in the isthmus.

I have had the glycogen content of the isthmus glands tested by one of my pupils, Dr. Herbert Simon, of Denver, Colorado, for it seemed to me of consequence to learn to what extent the glands of this part of the uterus are able to perform the biochemical function which devolve upon the corpus glands during the period pre-menstruum. Binder and Neurath investigated formerly, at my suggestion, the glycogen content of a number of uterine mucous membranes in various phases of the cycle, also of metropathic and adenomyotic uteri, and were able, along with other interesting details, to establish the fact that the glands in the pre-gravid phase revealed an uncommon wealth of glycogen. We may certainly regard this storage of carbohydrates as a fertilization of the mucous membrane, the purpose of which is to bring nourishment to the ovum imbedded in the mucosa for so long as it is left to the latter, that is, before the introduction of the maternal circulation. Simon, it is true, regularly found a rich storage of glycogen; but he found a uterus in which, in spite of a histologically undoubted developed pre-gravid phasic picture, there was, nevertheless, not any trace of glycogen in the distended and richly secreting glands. He found, further, a mucous membrane in which certain areas of glands revealed glycogen in quantity, while others contained very little or none at all. There are even glands which, in spite of the presence of a rich secretion, are not able to carry out the purposeful function of glycogen production. But it may be said in general that the pre-menstrual corpus gland produces and stores glycogen in large quantities. In the isthmus glycogen was not to be expected when

the mucosa was low and the glands were inactive. But in those cases in which the isthmus glands were distended and formed a microscopically demonstrable secretion, it was of interest to test the glycogen content. The formation of glycogen is an indicator of the preparedness of the mucous membrane to receive the fertilized ovum. In such cases Dr. Simon found the glands either entirely free from glycogen, or only sparse and very small nuclei were discoverable. These observations are to be published by Dr. Simon in another place. It is demonstrated, therefore, that in this regard also the mucous membrane of the isthmus must be designated as unfavourable for the embedding of the ovum.

It appeared to me important to follow out the comparison between isthmus and corpus in other phases of the monthly cycle. In doing so we notice very decided differences in the post-menstruum and the interval. I can show by microscopic preparations that in these phases also the limits of the isthmus are readily recognizable. This becomes clear if we place the microscopic discoveries along with each other, as illustrated by Fig. 4. We see here a post-menstrual mucosa.

The attentive observer will recognize here a clear bipartition of the mucous membrane in the corpus. In the depths the glands are pressed closer together, the stroma is woven more closely. The part of the mucous membrane nearer to the surface shows a much more loosely knit stroma, the glands are separated further from one another and, in traces, wider than in the depths. In the isthmus there is no sign of bipartition. The mucous membrane is apparently thickened in consequence of a cystic distension of the glands. There is no sign of a differentiation into two layers in this mucous membrane of the isthmus as in others of the same phase. In the corpus there is already indicated in this phase the superficial "predecidua" in early stages which will form later. In the isthmus nothing of the kind is to be seen.

In the interval too I have been able to establish in many preparations the great differences between corpus and isthmus. The mucous membrane of the corpus awakens to new life soon after menstruation. The differentiation of the mucosa into two, later into three layers, makes corresponding progress as the phase advances. I reproduce in Fig. 5 a mucous membrane of the first half of the interval in order to show how the stroma loosens in the superficial layers, the glands distend and begin to twist, and now the glands are sparsest nearest the surface. This is just the layer which becomes the "pre-decidual compacta" in the pre-

menstruum. Nothing of all this is to be found in the isthmus. The mucous membrane is here uncommonly poor in glands, the stroma closely woven and without any sign of a response to any hormonal stimulations. In the pre-menstruum a rudimentary reaction may set in, but may also be absent.

We see, therefore, that not only in the pre-menstruum, but also in all stages of the cycle, the differences between corpus and isthmus are very important, and it is not to be wondered at that, in the overwhelming majority of cases, delimitation with the naked eye should be possible in all phases. Let it be established, in conclusion, that the mucous membrane of the isthmus is in a position to react to hormonal stimulations, but to a much less extent than can the mucous membrane of the corpus. This concerns both the glands, which some times remain unaltered, and especially the stroma, which does not show any inclination to form a predecidual compacta. A menstrual haemorrhage from the mucous membrane of the isthmus is certainly possible, but equally certainly not the rule. We know that, after a supravaginal amputation which leaves the mucous membrane of the isthmus, there is generally no further menstruation. A long time ago, however, I pointed out that, if even only extraordinarily small portions of the mucous membrane of the corpus are left, menstruation may be maintained undisturbed for a long while. Since then I have been able to confirm this statement in several cases by clinical and microscopical observation. But the maintenance of the mucous membrane of the isthmus when carrying out a supravaginal amputation does not in any way guarantee the continuation of menstrual haemorrhages.

The relations of the isthmus to pregnancy have been very thoroughly explored. Indeed, one may say that the interest in the isthmus of the non-pregnant womb has arisen from interest in the lower uterine segment of the pregnant womb. Great services were rendered by Schmidt, Aschoff, and especially Stieve in the clearing up of many disputed questions of those days. Today we know that in the uterus in its earliest stage of pregnancy the upper and lower limits of the isthmus are as easily recognisable as in the pre-menstrual uterus. From the second month of pregnancy onwards the upper limit begins to disappear, becoming no longer recognizable in the third month. The whole isthmic portion of the womb is drawn into the ovum chamber (Stieve). Because of the active growth of the ovum this originally narrow portion of the uterus is extended, but only so far as the orificium isthmi inferius, which remains narrow as before and forms the boundary

between the corpus cavity plus isthmus, now filled and distended by the ovum, and the narrow cervical canal. We are speaking here simply of the orificium internum uteri gravidi. The so-called lower uterine segment proceeds from the isthmus. At birth this section thins and, along with the cervix, becomes a passive passage tube, while the substance of the corpus acts as expulsive muscle. The so-called contractional ring of the gravid uterus coincides with the orificium isthmi superius.

On the occasion of describing a uterus which enclosed an embryo, 84 mm. long, Stieve emphasizes that the skins of the ovum at the inner os uteri are not connected for an extent of about 16 mm. with the woven layer under them but rather lie directly upon the separated mucous masses. In advanced pregnancy, too, the soldering of the decidua capsularis with the decidua parietalis may be hindered in the area of the lower uterine segment, a condition which Stieve relates to the activity of the cervical mucous glands, some of which may cross the boundary of the inner os uteri. I have often noted, in the examination of numerous gravid uteri in various phases of pregnancy, that the distal pole of the ovum, that is its decidua reflexa (capsularis), was either quite loosely or not at all attached to the decidua parietalis, while higher up, the uterine cavity was entirely closed by complete adhesion. It may well be that the secretion of the mucous glands play a part here. In any case the anatomical difference of the decidua isthmi, and later of the decidua of the lower uterine segment in contrast with the remaining decidua parietalis corporis is of decisive importance for the incomplete or non-existent soldering of the capsularis of the lower pole of the ovum with the decidua of the lower uterine segment. I have pointed out earlier that, in the pre-gravid stage, a pre-decidual compacta is not formed in the isthmus. As the pars compacta of the decidua grows out of the pre-decidual compacta, the compacta remains undeveloped in the isthmus and later on in the lower uterine segment. That agrees very well with Stieve's very fine investigations. I believe that the quite loose or entirely absent soldering of the decidua capsularis of the lower pole of the ovum with the decidua parietalis in the lower uterine segment is connected with that, for the soldering in the higher zones of the uterus is completed just between reflexa and compacta deciduae parietalis. The reflexa is itself a compacta. Compacta, therefore, adheres to compacta. If the compacta is lacking, as is the case in the isthmus or in the lower uterine segment, the soldering is either loose or absent. That is of the greatest importance, on

the one hand for the necessary mobility of the lower pole of the ovum, on the other hand for the expansibility of the lower uterine segment *sub partu*. Were the lower pole of the ovum as firmly soldered to the decidua parietalis in the area of the lower uterine segment as is the case higher up, the distension of the inner os uteri, the projection of the lower pole of the ovum into the cervical cavity, and the alteration of the bowl-shaped lower uterine segment into a wide passive tube would thereby be hindered, and would only take place with considerable haemorrhage.

From these facts it is clear why the above described absence of a well developed pre-decidual compacta in the isthmus is of importance for the physiology of the pregnant and bearing uterus.

Part II.

The Supply of Arterial Vessels in the Isthmus.

In the first part of this work it was demonstrated that the isthmus uteri reacts little or not at all to the normal hormonal stimulations proceeding from the ovarium, and that the manifestations of the cyclical alteration of the mucosa of the corpus do not appear, or appear only imperfectly, in the mucous membrane of the isthmus. It was pointed out that, in consequence of the absence of a pre-decidual compacta in the mucous membrane of the isthmus during the pre-gravid phase, there appears during pregnancy a decidua whose compacta is either imperfectly or not at all developed, which is of considerable importance for the physiology of birth.

If all this is correct, and if the mucous membrane of the isthmus, though ranking with the mucous membrane of the corpus as regards its elements, at the same time lives its own life, it is then necessary to investigate whether the vascularization of the isthmus follows along with that of the corpus or whether it also reveals a certain independence. Variety of function would be difficult to reconcile with the idea of a unified provision of vessels.

The literature on the arterial vascularization of the uterus is well known to be very extensive, and it would seem, therefore, proper to review what has been written in order to ascertain whether material on this subject is to be found there. In fact, when the works most concerned are carefully gone through, there are found, partly in pictorial illustrations, partly in the text—though often between the lines rather than in downright description—indications regarding the question which interests us here.

Before all, I have, of course, studied thoroughly the well-known work of Redlich, "The Atlas of the Arterial Vascular System of the Uterus and its Appendages," Leipzig, 1911. It seems to me important to point out that the author, on the basis of the study of his injection (preparations which he prepared with gelatin and cinnabar, plaster of Paris and red lead) was able to recognize five variants in the course of the arteria uterina. He distinguishes:

1. A single arteria uterina.
2. Doubling of the arteria uterina.
3. Absence of a common branch at the angle of the uterus, and a division into a whole series of branches.
4. Cleavage of the arteria uterina.
5. Development of an arterial bend at the segment of the uterine angle in the corpus uteri.

One may not, therefore, expect *a priori* a unified behaviour of the isthmus vessels in all uteri investigated. From the Atlas mentioned let me quote just one observation: "So far as the details of supply of blood to the corpus uteri are concerned, the remark must be made that . . . according to Fredet . . . there exists between the arteries of the cervix and those of the corpus a scantily supplied zone: this view is in accord with my own X-ray graphs."

Freund, in his fine work "On the Theory of the Blood-vessels of the Normal and Diseased Womb," Jena, 1904, does not enter into details of the isthmus, but in Fig. 15 can be seen very clearly the provision of blood-vessels for the isthmus separated from the corpus.

With regard to the veins, Bayer expresses himself in the following terms: "In the neighbourhood of the corpus-cervix boundary . . . where the fibration takes a distinctly circular course, there is to be noticed as a rule a vein with a circular course. This ring-vein is not, however, so constant or always so clearly distinguished from others that it can be regarded as a trustworthy characteristic of the inner os uteri."

Very fine preparations have been demonstrated by Joachimovits before the Vienna Gynaecological Society. He used either mercury clarified with tetraline, or Teichmann's mass, or celluloidal colouring mixture as corrosional preparations. Two uteri he injected with 40 per cent iodipin and took X-ray photographs. He emphasizes the differing consistence of Hegar's zone of the uterus in contrast to the other portions of the organ, and

is thinking then as much of the musculature and elastica as particularly of the altered and increased vasculation.

Stieve describes in the cervix of the gravid uterus a compressible, non-erectile corpus cavernosum which is said to guarantee the closure of the cervix in the region of the inner os uteri during pregnancy, and also the shutting off of the uterine cavity after birth. He says: "The blood-vessels are present in far greater numbers in the wall of the cervix than in the wall of the isthmus. In the region of the inner os uteri the vessels form at the end of the third month a particularly extended weft composed of broad vessels."

Finally let us consider the publication of Davidsohn which appeared in Schwalbe's morphological works in 1893. He injected uteri and made preparations of the vessels. In several illustrations of non-gravid and gravid uteri can be seen very clearly the peculiar provision of vessels for the isthmus, that is for the lower segment of the uterus. Regarding a uterus in the eighth month of pregnancy the author says: "Immediately above the inner os uteri two arteries go to the right into the substance of the uterus, and just a little higher up two considerable branches, which are not inferior to those of the corpus . . . That we had to do here with arterial branches of the lower uterine segment was *a priori* clear . . . The result of the investigation was that the zone of the uterus which had to be regarded as the lower segment appeared to be well provided with directly approaching arterial vessels." Also with regard to the puerperal uterus Davidsohn emphasizes that the lower uterine segment receives its vessels just as directly as the corpus uteri. Although these fruits of reading are valuable they do not appear to me sufficiently to demonstrate these specific independent arterial provisions of the isthmus. I therefore injected 25 uteri in order to be able to judge this question myself. I selected barium sulfuricum as the substance for injection and prepared constantly fresh emulsions having the consistence of fairly thick buttermilk. It appeared to me advisable to make the first material to be injected into the vessels rather thinner. I particularly refrained from washing out the vessels with any kind of liquid before proceeding with the injection. It proved advisable to extract from the cadaver not only the genital but also the bladder and the rectum so that a small piece of the arteria hypogastrica was at my disposal for the introduction of the cannula.

Dr. Stefan Simon took the X-ray photographs, for which I should like to express my thanks to him. After fixation and opening of the preparation the outer boundaries of the uterus, as

well as the contours of the uterine cavity, were marked into the X-ray graph. The boundaries of the isthmus were brought out by two horizontal lines.

As Redlich has already emphasized, the arteria uterina shows distinct variants. It should not be surprising then if the area of the isthmus is provided with arteries in a good many different ways. That the isthmus shows a specific zone of vessels appears most clearly in such uteri as the one reproduced in Fig. 1. We see here the organ of a nullipara; the arteria uterina approaches the angle of the uterus at the level of the proximal orificium isthmi, mounting here at a sharp angle parallel to the side of the uterus without revealing any winding at all. In the area of the isthmus there pass fine vessels, arranged in bunches and almost parallel, penetrating transversely into the substance of the uterus from a loop of the arteria uterina lying far outside the uterus. We cannot by any means assert that the isthmus is in any way worse fed with blood than the corpus. But certainly the provision of vessels for the isthmus must be recognized as an individual and a separate one.

The supply of blood by a special ramus isthmicus is uncommon, but it does occur (Fig. 2). The uterus of a nullipara shows here in the area of the corpus, numerous vessels leaving a sharply winding arteria uterina, running parallel, penetrating into the uterus and ascending gently towards the fundus while the cervical vessels run only transversely. The ramus isthmicus springs from a stronger cervical branch of the uterina. Keen observation reveals that behind the thicker ramus isthmicus a finer branch belonging to the posterior wall runs in the same direction. In any case one may speak with full right of a special provision of the isthmus. Whether the isthmus receives thereby less blood than the corpus or the cervix appears very questionable.

With greater justification this can be asserted regarding the uterus in Fig. 3. The metropathic uterus of a multipara shows a great number of strongly twisted corpus branches which rise gently towards the fundus. The cervix is provided for by less ample vessels which descend obliquely. The vessels of the isthmus are sparse and short and end at least in the portions of them filled with the emulsions near to the angle of the cervix. In this uterus the isthmus is a decidedly sparsely vasculated section.

The same statement is true of the uterus reproduced in Fig. 4. We are concerned here with the asymmetrically formed and closed womb of a multipara. The cervix is lengthened, the cervical

canal widened in contrast with the richly sufficiently blood-nourished cervix, the isthmus, the arteries of which end not far from the angle of the cervix, appears relatively poor in vessels.

There are indeed uteri in which this special provision of vessels of the isthmus stands out less clearly as, for example, in Fig. 5. But upon attentive observation, the shorter and transversely running branches of the isthmus can be contrasted with the upward striving of the branches of the corpus and the downward striving branches of the cervix. It is true that the autarchy of the isthmus is not so evident here as in the previously described preparations.

I may perhaps reproduce here (Fig. 6) from the work of Davidsohn one of his figures, which shows very clearly that corpus, isthmus, and cervix are provided for by three separate groups of vessels.

The isthmus of the non-gravid uterus is apparently less richly vasculated, as a rule, than the corpus and the cervix. However, so many physiological and pathological influences are at work here that we cannot be surprised if we occasionally perceive a very richly vasculated isthmus. But it can be established by injected uteri that, with few exceptions, the provision of the isthmus is a distinct and individual one. Of course all injected branches spring from the arteria uterina. But the isthmic zone of the womb receives its branches from its proper group of vessels, which in certain cases may be variously shaped.

The distinct provision of vessels for the isthmus is in harmony with the individual physiological life of this section of the womb.

Part III.

The Isthmus in the Pathologically Altered Uterus.

Seeing that the behaviour of the isthmus in pregnancy and birth has been so excellently studied and understood it is the more remarkable that so little work has been done regarding the fate of the isthmus in diseases of the non-pregnant womb.

Aschoff related the pathological alterations of position (I think that the word alterations of attitude would be more in place) to a weakness of the region of the isthmus. Hegar considers the isthmus in the infantile uterus to be both relatively and absolutely lengthened; also that a stretching of the isthmus plays a part in the elongation, a statement which is confirmed by Nürnberger. Novak and Graff find the mucous membrane of the isthmus changed into squamous epithelium in a woman suffering from war-amenorrhoea. That is about all there is to report from works

concerned with the subject. Nürnberger, therefore, says with full justification "concerning the behaviour of the isthmus in inflamed conditions of the endometrium as well as concerning the question of genesis of carcinoma and other things besides, there do not exist to-day any systematic investigations." Sternberg, too, feels the gap which yawns here and finds it desirable to "investigate the pathology of the uterus from the standpoint of its triple division." For a long time I have turned my attention to the behaviour of the isthmus in pathological alterations of the uterus, and have been collecting material on the subject for more than five years. Naturally it seemed to me to be of immediate interest to investigate the mucous membrane of the uterus in those conditions which go along with strong thickening of the mucous membrane of the corpus. That is in hormonal disturbances which lead to hyperaemia, to oedema, and to hyperplasia of the mucosa of the corpus. We may accept to-day with the greatest probability that in haemorrhagic metropathy morbid endocrine influences act upon the mucous membrane of the uterus. While normally, in the first stages after conclusion of menstruation, the folliculin brings about an improvement in the supply of blood but causes no hyperaemia, and in the second half of the interval the luteo-hormone, particularly in the pre-menstruum, causes a very copious supply of blood through one partial factor (hyperaemin) and through another (progestin) causes the typical pre-menstral glandular change, in haemorrhagic metropathy the action of the luteo-hormone fails completely, while the action of the folliculin takes place excessivley both in intensity and duration. Hyperaemia, or oedema, very frequently hyperplasia of the mucous membrane are the local symptoms that follow. I can certainly say that I have seen, in the course of a 25 years' occupation with gynaecological pathology, countless uteri with hyperplastic mucosa. Sometimes the degree of hyperplasia was so great that the mucous membrane gave the impression of there being a collection of polypi pressing thickly together, in other cases the macroscopic appearance might mislead one into a diagnosis of cancer. But up to the present I have only twice seen the mucous membrane of the isthmus show hyperplasia to a marked extent. In all the remaining cases—I cannot reckon them, but the number is very great—the hyperplasia was confined to the mucous membrane of the corpus. Fig. 1 shows a uterus with hyperplastic mucous membrane of the corpus.

The histologically verified isthmus is very long. The mucous membrane there is very thin. It does not share in the hyper-

plasia in the slightest degree. In Fig. 2 the delimitation of the isthmus is very clearly visible. The mucous membrane of the corpus shows really big protuberances and overhangs the isthmus a little. The mucous membrane of the cervix overtops the level of the mucosa of the isthmus and is bounded towards the latter by a low fold.

Specially interesting is the discovery in the uterus, Lab. Prot. No. 38597. The mucous membrane of the corpus is thick, soft, shaggy, hyperplastic. But its areale is narrowly limited, its cranio-caudal diameter is small. So much the larger is the isthmus, the upper and lower boundary of which is drawn uncommonly sharp. The mucous membrane of the isthmus is quite thin but strongly insanguinated.

Repeatedly I have observed, even when a positional anomaly was not present, a thick oedematous mucous membrane without the histological signs of a hyperplasia, and without indication of a myoma or an inflammatory appendage tumour. The pathological congestion of blood following upon abnormal hormonal influence may be revealed by an oedema of the mucous membrane, as is photographically reproduced by Fig. 3.

The oedema may spare isolated parts of the endometrium. The mucous membrane of the isthmus, however, has remained thin throughout and therefore ends sharply at the orificium isthmi superius. I add, also, the slide of a Tetrander section (Fig. 4) which allows one to observe the enormous difference between the thick oedematous mucous membrane of the corpus and the thin, non-oedematous mucous membrane of the isthmus. The mucous membrane of the corpus corresponds to the second half of the interval, but is not yet pre-gravid. The stroma is considerably loosened by oedema. The borderline towards the isthmus falls steeply. The isthmus is relatively long, its mucous membrane quite thin. In the cervix are some small cysts.

The macroscopically visible boundary between the hyperplastic mucous membrane of the corpus and the mucosa of the isthmus may be very variously shaped. In the slide representing Fig. 5 may be seen a hugely thickened, polypoid hyperplastic mucous membrane.

As, in consequence of basal hyperplasia, it appears fairly deeply sunk into the musculature, the transition from the thick mucosa of the corpus to the mucous membrane of the isthmus, which has remained quite thin, seems to be a quite gradual and gentle descent. The isthmus here is very short, the mucous mem-

brane without signs of hyperplasia, poor in glands and uncommonly thin.

Fig. 6 shows the slide of a Tetrander section derived from a uterus with hyperplastic mucosa of the corpus. Superficially examined, the mucous membrane appears to lie here quite on a level with the mucous membrane of the isthmus. This is due, on the one hand, to the relatively deep penetration of the basal hyperplastic mucous membrane in the musculature of the corpus; on the other hand, the mucous membrane of the isthmus is here somewhat thickened, and there are traces of hyperplasia. In Fig. 7, on the other hand, we see a gradual sinking of the hyperplastic mucosa of the corpus towards the mucous membrane of the isthmus, which contains a great number of small cysts, a part of them deeply imbedded. Finally, Fig. 8 reproduces the histological picture of a hyperplastic mucosa of the corpus with superficial necrosis. Next to it is the thin mucous membrane of the isthmus with sparse, narrow glands, without signs of hyperplasia.

On the basis of these briefly described phenomena, we may say in general that, with few exceptions, the mucous membrane of the isthmus shows not at all, or only in traces an odema or hyperplasia of hormonal origin, while the mucous membrane of the corpus is subject to considerable thickening. The mucous membrane of the isthmus has considerably less capacity than the mucosa of the corpus of reacting to physiological hormonal excitations. The same applies to pathological endocrine influences. It cannot be dogmatically laid down, however, that hyperplasia of the mucous membrane of the isthmus never occurs, for there are exceptions, although these are infrequent according to my experience.

It is quite possible that, in cases in which the hyperplastic mucous membrane reaches to the inner os uteri, that is, to the orificium isthmi distale hormonal processes are not at all concerned. Presumably it is a question here of uteri with essential hyperplasia of the mucous membrane unconditioned by endocrines in Weibel's sense, of growth impulses which apply to the mucosa of the corpus as much as to that of the isthmus.

In consequence of these experiences it was incumbent upon me to examine the relations in adenomyosis uteri interna (adenomyosis of the mucous membrane) to see whether the mucous membrane of the isthmus is capable of adenomyosis or not. Only a short while ago I carefully described my material (Weitere Beiträge zur Klinik und Bemerkungen zur Pathologie der Adenomyosis Uteri, *Zentralblatt für Gynäkologie*, 1932, Part

13, and Adenomyosis uteri, *The Irish Journal of Medical Science*, Special number, June, 1932). I have at my disposal over 148 uteri with adenomyosis of the mucous membrane. I will say at once that I have seen the region of the isthmus adenomyotically diseased in only one case. I am first of all not in a position to say whether the islands of mucous membrane lying intramuscularly have proceeded from the mucous membrane of the isthmus or derived from the mucosa of the corpus, and have pushed forward obliquely downwards into the area of the isthmus. In spite of everything I cannot exclude the possibility that in this case the glands of the isthmus have supplied the germs of mucous membrane lying deep in the musculature. In all other cases such behaviour can be excluded from consideration. Instead of long disquisitions I reproduce here some lantern slides of Tetrander sections. Fig. 9 shows the area of the isthmus of the uterus of a 47 year-old woman. The womb was 12 centimetres long. The musculature is considerably thickened and coarse, the mucosa, thick, soft and hairy. Even as a macroscopical investigation, the exceptional length of the isthmus struck one. The microscopic investigation revealed the existence of a hyperplastic mucous membrane which sank sharply towards the orificium isthmi superius. From the mucosa of the corpus there extend into the depth, islands lying intramuscularly and running obliquely from internally below to externally above. The area of the isthmus is free from adenomyotic islands.

Things are arranged similarly in Lab. Prot. No. 7520. Here a uterus only eight centimetres long, of a 48 year-old woman shows a thoroughly coarse myometrium, the endometrium being thin, smooth, insanguinated. The mucous membrane corresponds to the interval. The intra-muscular islands of mucous membrane frequently containing cystically dilated glands ramify from the mucosa of the corpus and rise obliquely from internally below to externally above to the upper boundary of the isthmus. From the mucosa of the isthmus, thin and poor in glands, no glands run out.

Conditions are particularly clear in the next preparation which I reproduce in Fig. 10. Here exists an adenomyosis in the cranial sections of the corpus. The isthmus is completely free.

The cervix is adenomyotically altered. The nine centimetre long uterus of a 45 year-old woman appears very coarse, the mucous membrane is thin and smooth. The adenomyosis of the corpus is confined to the sections of the womb lying more

cranially and is not demonstrable in the portion of the Tetrander section reproduced here on the lantern slide. The cervix is, however, certainly the seat of an extended adenomyosis of the mucous membrane. The histological picture of the cervical adenomyosis agrees completely with Fig. 168 of R. Meyer in the handbook of Henke and Lubarsch Vol. VII, Part 1. The mucous membrane of the isthmus is very thin and poor in glands, the musculature under it, is entirely free from islands of mucous membrane.

We see, therefore, that at least in the overwhelming majority of all cases of adenomyosis of the uterine mucous membrane, the isthmus is found to be free from islands of mucous membrane and that, at the most exceptionally, the mucous membrane of the isthmus can become capable of adenomyosis. Among my preparations there is not one which can demonstrate an actual ability of the mucosa of the isthmus to send glands and stroma into the musculature of the isthmus. I should not provisionally exclude such a possibility altogether, since the one case mentioned above was not examined in serial sections and because, although seldom and in a moderate degree, an exophytic hyperplasia of the mucous membrane of the isthmus can indeed occur. The clinics of adenomyosis indicate that hormonal processes can play, if not indeed a causative then at least a promoting or hindering role. Our discoveries in the isthmus of adenomyotic uteri agree very well with the small reactional capacity of the mucosa of the isthmus to hormonal excitations which has been emphasized above.

A very brief account will be given of the behaviour of the mucosa of the isthmus in the presence of endometritis. First of all, a remark on the macroscopic appearance of the inflamed mucosa of the corpus. The inflamed endometrium of the corpus is often described as diffusely thickened, or as thick and uneven. I think that confusion has taken place here partly with pre-gravid, and partly with hyperplastic endometria.

The chronically inflamed endometrium can be either thin or thick according to the phase existing at the moment. The inflammation may be recognized by the quite finely nodulated surface which is best characterized by saying that the mucosa looks as if it were strewn with sand. If such wombs are opened carefully it is seen at the first glance that the mucous membrane, covered as it is with the elevations shaped like sand-grains and generally also reddened, extends from the fundus at least as far as the orificium isthmi caudale. The mucosa of the isthmus is correspondingly thinner than that of the corpus, but also sown

with the finest unevennesses. I have set up the macroscopic preparations of this kind, for the inflammation of the isthmus is easily recognizable even in the preserved specimen.

The infiltration of round cells and plasma cells, in older cases the cicatrized alteration of the stroma in the isthmus are as easy to recognize as in the mucosa of the corpus. As was to be expected *a priori*, the inflammation by no means stops at the isthmus but alters its mucous membrane in the same way as the endometrium of the corpus reacts to excitations which condition inflammation.

I have had occasion also to establish the like behaviour in tuberculous uteri. Tuberculosis of the endometrium extends unhindered over the mucous membrane of the isthmus. Isolated or conglomerate tubercules are found in the mucosa isthmi. It is true that I found in one case of advanced tuberculosis of the mucosa of the corpus, the mucous membrane of the isthmus and the cervix free from tubercules.

Finally, let me deal with the relations of the isthmus to carcinoma of the corpus. I must forego a description of the behaviour of the isthmus in cancer of the collum. I have not yet been in the position to deal with this portion of the subject exhaustively as our material suffers from the operational technique applied. I require a great many more preparations in order to be able to judge the subject definitely. I can, on the other hand, say the following on the relations of carcinoma of the corpus to the mucosa of the isthmus. We can adjudge to the mucous membrane of the isthmus powers of resistance to a certain degree against carcinoma of the corpus, for, not only macroscopically but also microscopically, we very often see that the neoplasm ends at the upper boundary of the isthmus. This power of resistance is of course limited, and the cancer seizes upon and destroys the mucous membrane of the isthmus also after a certain period. I have been able to recognize three types which shall be briefly described.

In the case Prot. No. 43452 we see a uterus with carcinoma of the corpus. It is eight centimetres long and thin-walled. In the cavity of the corpus sits a flat sod-shaped papillary carcinoma which obviously has already ceased the musculature. On macroscopical investigation the neoplasm of the mucosa of the corpus seems to stop sharply at the cranial end of the isthmus. In reality, however, the glands belonging to the isthmus are no longer typically built, but already betray clearly cancerous alterations.

A second type is represented by Lab. Prot. No. 47164. The

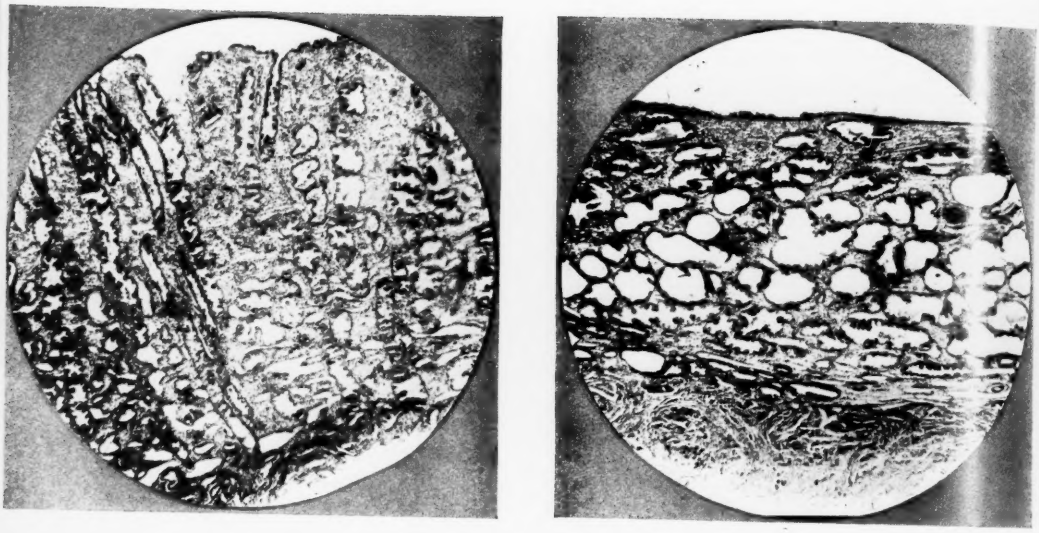
macroscopic picture of this neoplasm is about the same as in the preceding case. Here, too, the edge at the orificium isthmi superius is macroscopically fairly sharp. But on microscopical examination the fact was revealed that under the mucous membrane of the isthmus a considerable number of partly glandular, partly solid foci, have grown under the still normal glands.

A third type is represented in Fig. 11. We are concerned here with the eight centimetre long uterus of a 50 year-old woman. In the cavity of the corpus is to be found an irregular humpy, partly polyp, partly sod-shaped tumour mass which proves to be primarily glandular but for wide stretches secondarily solid, occasionally mucus forming carcinoma of low maturity. The upper end of the mucous membrane of the isthmus is overlaid by a peak-shaped continuation of the carcinoma. The microscopical investigation reveals the picture which is represented in three micro-photographs (Fig. 12). In the first picture (A) the neoplasm is seen closely attached to the mucous membrane of the isthmus. There has taken place here complete cohesion of the carcinoma with the surface of the mucous membrane. It would not be long before the mucous membrane was entirely destroyed. In the second picture (B) is seen a more caudal part of the isthmus. The carcinoma is overlying the mucous membrane, whose epithelium is still preserved in parts. Here contact only has been reached, but not yet cohesion or invasion. In the third picture (C), which corresponds to parts of the isthmus lying still further caudally, the mucosa of the isthmus is over-roofed by the carcinoma. A contact probably existed here *in situ naturali*, not at all, or only temporary.

I am very conscious that I have not in the preceding exposition dealt exhaustively with the important subject of the physiology and pathology of the isthmus. Much has still to be done and I am still occupied with further studies. It was my task to throw light upon a department of pathology which has hitherto been all too little worked upon and in which there is assuredly still much of interest and of practical utility to be sought and found. If the foregoing lines should stimulate others to this task, then the labour I have spent upon it hitherto will not have been wasted.

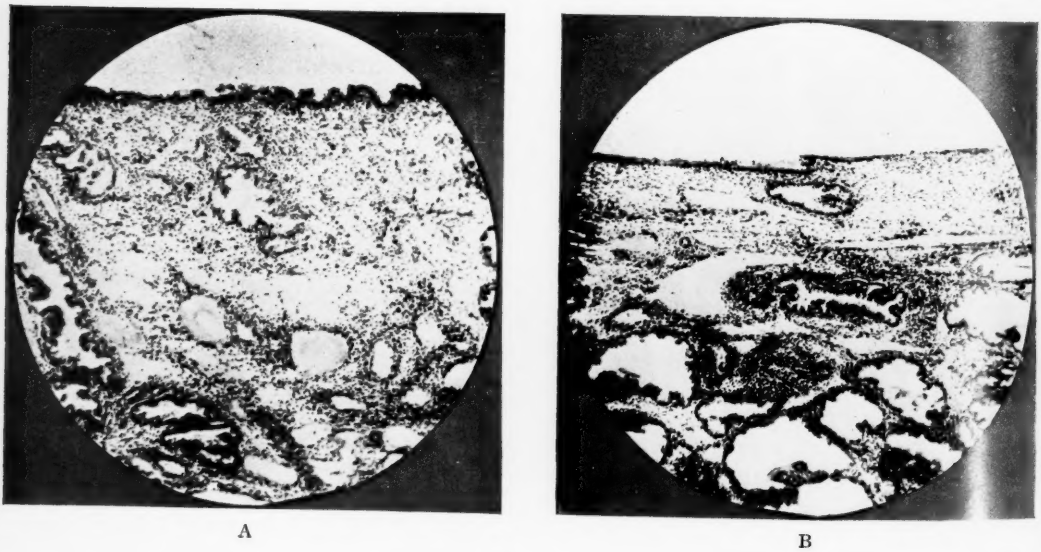
PART I.

FIG. 1.



A B

FIG. 2.



A B

FIG. 3.

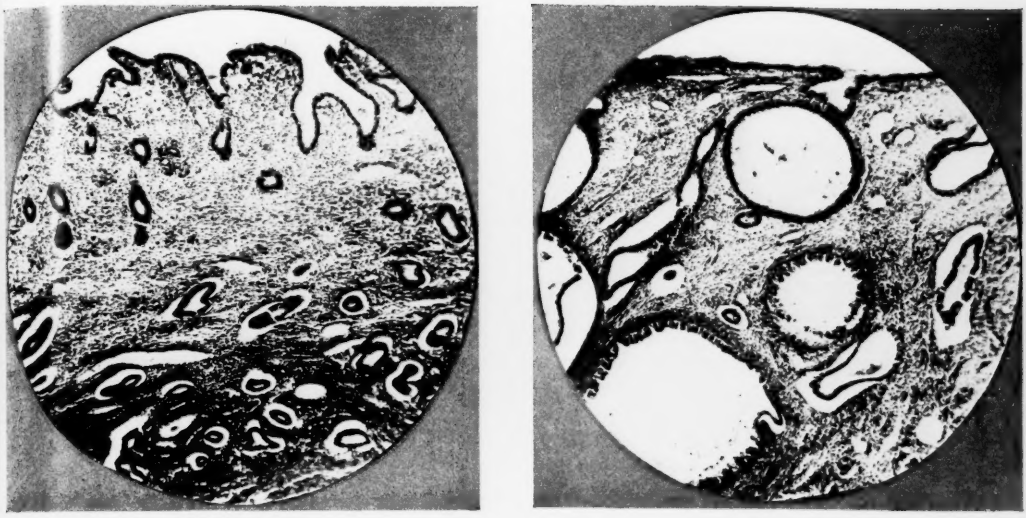


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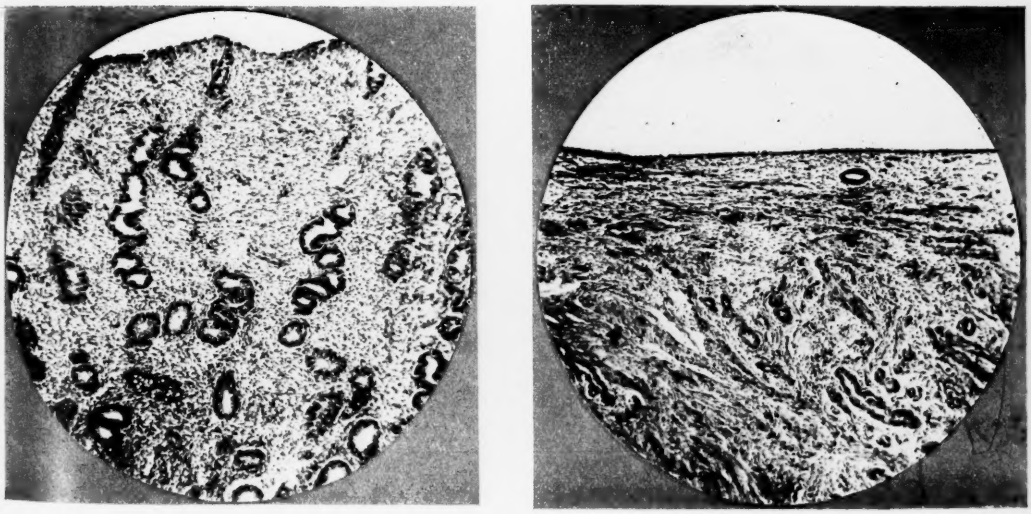
FIG. 4.



A B

FIG. 5.

MINN. OF W/OH.

FIG. 1.

FIG. 2.

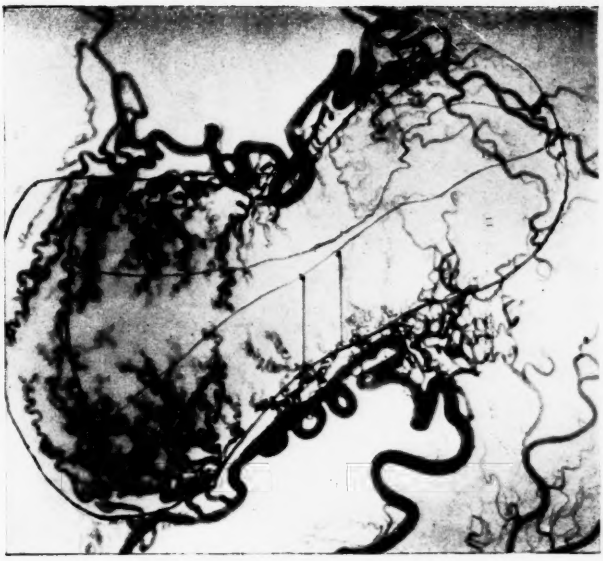


FIG. 4.

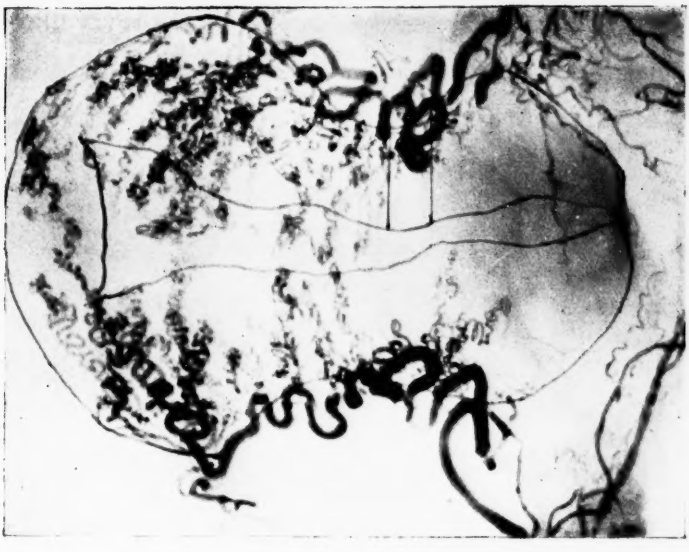


FIG. 3.

UNIV OF IOWA

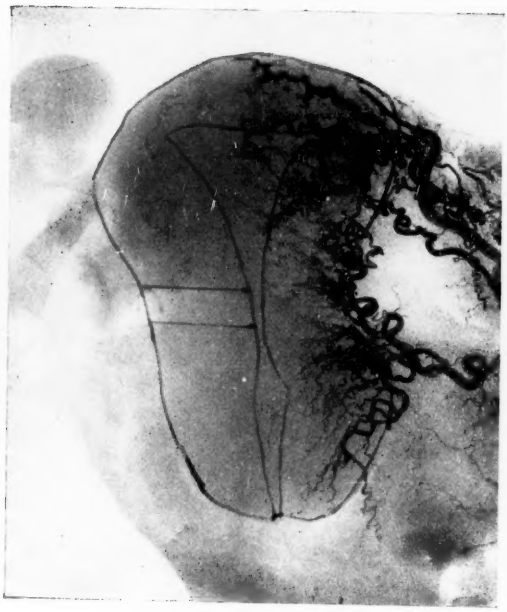


FIG. 5.

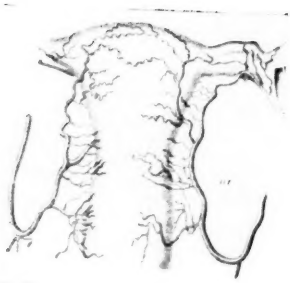


FIG. 6.

PART III.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

OHIO STATE OF

FIG. 5.

FIG. 6.

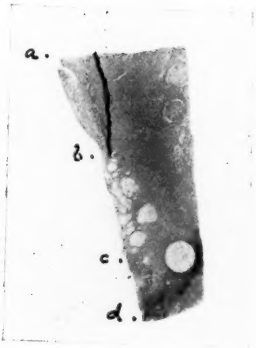
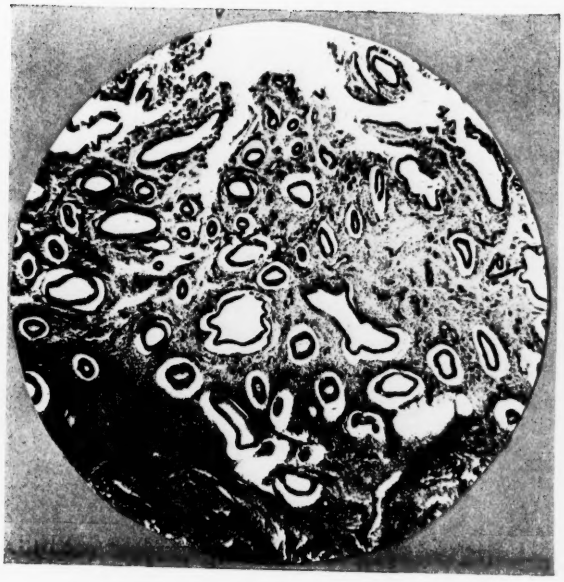
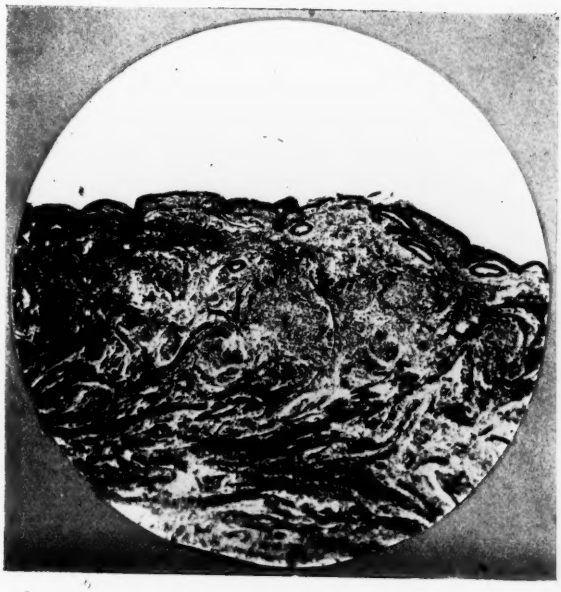


FIG. 7.



A



B

FIG. 8.

FIG. 9.

FIG. 10.

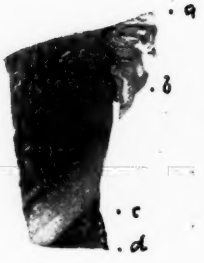
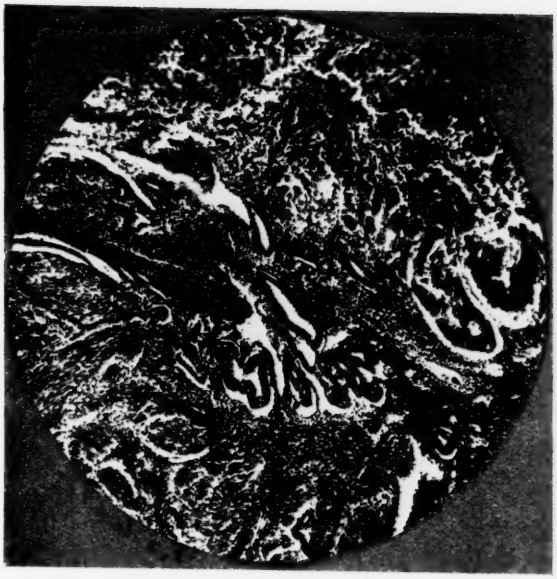


FIG. 11.



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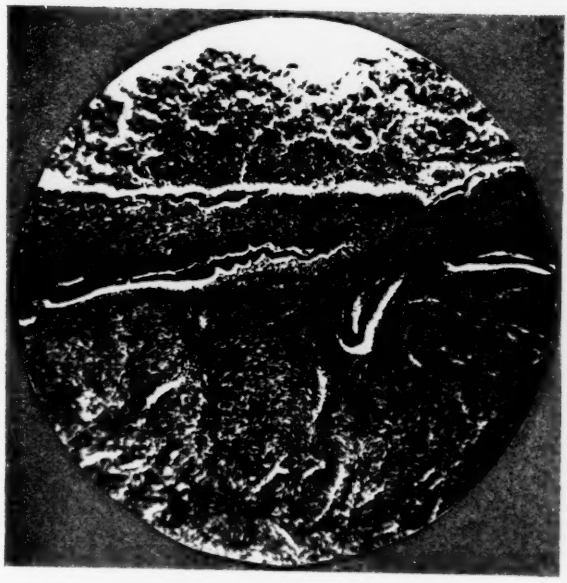

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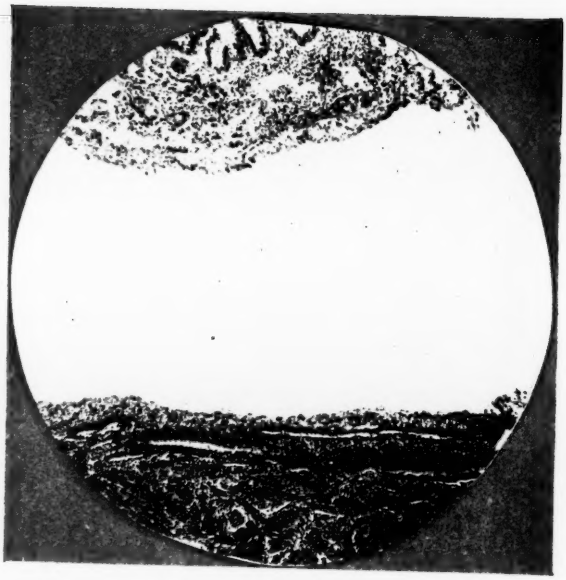
FIG. 12.



C

FIG. 12.

Description of Plates
Part I.

Fig. 1.
Lantern slide of a Tetrander section, pre-menstrual phase. Lab. Prot. No. 28199. a–b—mucosa of the corpus, b–c—mucous membrane of the isthmus, c–d—mucosa of the cervix. Similar lettering in all the following slides of microscopic preparations.

Fig. 2.
Pre-menstrual phase. A—corpus, B—isthmus. Lab. Prot. No. 43699. Zeiss magnification.

Fig. 3.
Surface of the mucous membrane, pre-gravid uterus. A—corpus, B—isthmus. Lab. Prot. No. 43699. Zeiss Lens A.

Fig. 4.
Post-menstrual mucosa. A—corpus, B—isthmus. Lab. Prot. No. 47250. Zeiss lens A

Fig. 5.
Mucosa of the interval. A—corpus, B—isthmus. Lab. Prot. No. 26917. Zeiss lens A.

Description of Plates
Part III.

Fig. 1.
Hyperplasia endometrii. Lab. Prot. No. 22179. The isthmus between the two lines.

Fig. 2.
Uterus with hyperplastic mucous membrane of the corpus, isthmus without share in it. Lab. Prot. No. 26082.

Fig. 3.
Oedema endometrii. Lab. Prot. No. 37975.

Fig. 4.
Uterus with oedematous mucous membrane. Lettering as in Fig. 1, part I. The boundary of the mucous membrane drawn in black against the musculature. Lantern slide of the Tetrander section. Lab. Prot. no. 40513.

FIG. 5.
Hyperplasia endometrii polyposa. Lab. Prot. No. 43387. Lantern slide of the section.

FIG. 6.
Hyperplasia endometrii cystica. The mucous membrane of the isthmus slightly thickened. Lantern slide. Lab. Prot. N. 45750.

FIG. 7.
Hyperplasia endometrii. Isthmus with cystic mucous membrane. Lantern slide. Lab. Prot. No. 41313.

FIG. 8.
A—hyperplastic mucosa of the corpus, B—mucous membrane of the isthmus, thin, poor in glands. Zeiss lens A. Lab. Prot. No. 34602.

FIG. 9.
Adenomyosis uteri interna. Lantern slide. Lab. Prot. No. 45285.

FIG. 10.
Adenomyosis corporis et cervicis. Lantern slide. Lab. Prot. No. 39641.

FIG. 11.
Carcinoma of the corpus, roofing over the cranial end of the mucosa of the isthmus. Lantern slide. Lab. Prot. No. 46222.

FIG. 12.
Carcinoma of the corpus. A—overgrowing the mucous membrane of the isthmus, B—overlying the mucous membrane of the isthmus, C—overroofing the mucous membrane of the isthmus. Lab. Prot. No. 46222. Zeiss lens A.

(*The discussion on this paper will be found on page* 533.)

Uterine Inertia.

BY

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IF the disasters of midwifery could be traced back to their primary cause it is probable that the majority of them would ultimately be ascribed to a failure in the dilating and expulsive forces of the uterus. Feeble contractions are the chief cause of delay, and the consequent interference to expedite labour. This in its turn, especially if unwisely applied, may be a cause of lacerations, haemorrhage, and sepsis. A feebly acting uterus is unable to flex and rotate the child from the occipito-posterior position, or force down the soft breech; in both cases assistance by internal handling is required. How many times in dealing with ante-partum haemorrhage, for example, have we prayed for contractions to be strong and efficient and, while watching the slow progress of labour in a patient with a flat pelvis, have we not predicted adequate moulding and a safe delivery if contractions would only become regular and strong? It is needless to add that the long drawn-out pain and anxiety of inertia makes the memory of labour a nightmare both to the mother and her husband.

For the child the long labour is a considerable risk, and not a few lose their lives through the exhaustion of the process. In short it is not too much to say that uterine inertia is the *fons et origo* of a large number of the serious troubles and even fatalities of obstetrics.

Clinical Summary of 49 Cases of Genuine Inertia.

It was felt that some useful purpose would be served if the clinical histories of a series of cases suffering from primary uterine inertia was to be analysed.

The case records of over 4,500 consecutive deliveries at Queen Charlotte's Hospital were searched, and all cases in which the first stage of labour lasted for more than 48 hours were classed as "Long labours." In each of these cases a detailed analysis of the available facts was made.

It was found that among these 4,500 women, there were 268 who had long labours as judged by this standard. This group of cases was further analysed with the object of discovering the cause of the prolonged labour, with special reference to the *role* played by weak pains in the prolongation of labour, and the dangers resulting from primary uterine inertia.

The cases were divided into two groups after eliminating 65 cases due to some form of obstruction:

Class A. The contractions were not good, and some of the patients were undoubtedly suffering from mild inertia; while in others an element of disproportion could not be eliminated.

From the 268 cases of delayed labour collected 154 cases were placed in this group.

Class A (154 cases).

Table I.

Mild inertia—occiput anterior.		
Length of first stage 48–60 hours ...	73	
,, ,, ,, ,, 60–72 hours ...	21	
,, ,, ,, ,, 72–84 hours ...	16	
		110
Persistent occipito-posterior position ...		33
Hydramnios		5
Twins		6
		154

Class B: Genuine cases of primary inertia.

The delayed labour being solely due to ineffectual uterine contractions, with or without rigidity of the cervix.

In this category were placed 49 cases; in 13 of the cases the cervix was mentioned as being definitely rigid.

It is with these 49 cases of genuine inertia that this clinical summary will deal.

Incidence. The fact that only 49 cases occurred in 4,500 labours shows that the condition is not common. Further, when inquiring into the origin of these 49 cases it was found that

27 were "Booked" cases.
22 were "Emergency" admissions.

The incidence of severe inertia in hospital practice can be estimated from the "Booked" cases, 27 cases of inertia occurring among 4,137 "Booked" cases. This gives an incidence of one in 150.

As a factor complicating emergency admissions, however, inertia was more common, 22 out of 396 "Emergency" admissions being cases of primary inertia, an incidence of one in 18.

Age. The age incidence was as follows:

TABLE II.
Age Incidence.

Under 20	6
20–30	27
30–40	14
Over 40	2
	49

Social. Inertia occurred rather more frequently among married than among single women. This was estimated from the fact that 800 single women were delivered during these years.

TABLE III.
Maturity

8	cases were premature.
36	cases were at term.
5	cases were post-mature
49	

It appears that inertia was not influenced by maturity, although further reference will be made to this when induction of labour is considered.

TABLE IV.
Parity.

43	patients were primiparae
6	patients were multiparae.
49	

The incidence among the primigravidae delivered was one in 60, and among the multiparae one in 300; the condition being five times as common in primigravidae as in multiparae.

It has been stated by some authorities that inertia is likely to recur in subsequent labours. It was found, however, that five of the six multiparae who suffered from inertia did not have any evidence of inertia in previous labours. Information was not available in the sixth case.

TABLE V.

Presentations.

Left occipito-anterior	...	23
Right occipito-anterior	...	11
Left occipito-posterior	...	8
Right occipito-posterior	...	3
Twins	...	1
Right sacro-anterior	...	3
		49

From this table it appears that severe cases of inertia are not only due to malpresentations, and that any presentation may be present.

TABLE VI.

Antenatal complications.

Normal pregnancy	...	36
Albuminuria ...	...	9
Hydramnios ...	...	2
Cardiac failure ...	...	1
Phthisis ...	...	1
		49

It was found that 13 cases presented abnormalities during the latter half of pregnancy, and in this series there appears to be an unduly high number of cases of albuminuria.

Induction. In 13 of the 49 cases of inertia, induction of labour was performed. Inertia followed induced labour more often than spontaneous labour. There does not seem to be any connexion between inertia and the method of induction.

Rupture of the membranes. The membranes ruptured prematurely in 30 out of 49 cases; this appears to have definite connexion with the inertia.

TABLE VII.

Length of labour.

First stage. In 17 patients the first stage lasted for over 100 hours.

Second stage.

Under two hours ...	24
Two to three hours ...	14
Over three hours ...	9
	47

In two cases the cervix never dilated fully.

Third stage.

Under thirty minutes ...	40
Over one hour	8
Died before delivery of placenta	1
	49

Post-partum haemorrhage.

Eight patients lost over 20 ounces of blood

Manual removal of placenta.

This was performed eight times.

The second stage was often normal after an inert first stage; in nine cases only was the second stage unduly prolonged, although the interference often required tended to shorten this stage.

The third stage showed a high rate of manual removal of the placenta; owing to non-separation.

TABLE VIII.

Method of delivery.

No assistance	22
Forceps	12
Manual rotation and forceps	7
Perforation	6
Assisted breech	1
Died undelivered ...	1
	49

It will be seen that less than half the cases ended in spontaneous delivery, and attention is drawn to six cases that ended in perforation, a not infrequent termination of severe inertia, complicated by rigidity of the cervix.

The children. Apart from the high percentage of stillborn children there does not appear to be any connexion between

the weight and sex of the children born, and the occurrence of inertia.

TABLE IX.
The children.

Death-rate.		
	Alive	29
	Stillborn	18
	Neonatal deaths	3
		50
Birth weight.		
	Under six pounds ...	14
	Six to nine pounds ...	32
	Over nine pounds ...	3
		49
	Not stated	1
		50

TABLE X.
Treatment.

Expectant	5
Sedatives only	27
Pituitrin and sedatives ...	11
Castor oil and enema ...	2
Manual dilatation of cervix	2
De Ribes' bag	1
Willett's forceps to child's scalp	1
	49

It will be seen that the practice at Queen Charlotte's Hospital is chiefly expectant. In two cases only was manual dilatation of the cervix performed.

TABLE XI.
Results of inertia.

Deaths (two booked, three emergency cases).	
Puerperal sepsis ...	3
Chloroform poisoning ...	2
	5

= 10 per cent mortality.

Morbidity (Ministry of Health Standard).

Deaths	5
Local uterine sepsis ...	9
White leg	2
Septicaemia	2
Parametritis	1
	19

It has already been seen that if the results of inertia are serious for the child, they are no less serious for the mother. A death-rate of 10 per cent, and a morbidity-rate of 40 per cent testify to this.

It is natural, therefore, that much investigation and speculation should have been brought to bear upon the clinical problem. But a moment's thought reveals its complexity. Before we can describe the cause of inertia, much less prescribe the treatment, we should know the origin and mechanism of uterine contraction. But of this elementary physiology we have very little certain knowledge. Any real investigation of inertia should, therefore, begin far back in the cause of the onset of labour.

During late pregnancy it is well known that the uterus contracts rhythmically and palpably, but it is perhaps not so well known that, when recorded on a moving paper by means of a manometer registering changes of intra-uterine pressure, the strength of the contractions during pregnancy may be similar to that during the first stage of labour.

We have a graph which is a record of intra-uterine pressure at 36 weeks of pregnancy of a patient who had three children. A small, narrow bag on the end of a hollow gum elastic catheter was introduced, the patient being anaesthetized with gas and oxygen. Before the first dose of two units oxytocin (pitocin) there were uterine contractions indistinguishable from those of a slow first stage labour. After oxytocin had been given the uterus acted regularly and rather frequently, but beyond a little sensation in the back for 10 minutes the woman stated that she had not had any labour pains, nor did she have for the whole of the tracing. In fact it is not possible to say, by an inspection of the tracings, whether the uterus is in labour or not. These contractions, however, similar as they are to those of the early stages of labour, are not felt by the patient, nor do they dilate the cervix. The contractions during pregnancy are followed by complete relaxation, but our tracings show that the relaxation

of the fundus is just as complete between the contractions of the first stage of labour.

If therefore, the fundal contractions during pregnancy and labour are similar, when examined on tracings, is it possible that the essential element in the onset of labour is less the occurrence of some new activity of the fundus than an active relaxation of the cervical ring of muscle? We are reminded here of the analogy of spasmodic dysmenorrhoea in which there is a failure of relaxation of the circular fibres of the internal os. It is clear that there are two definite uterine actions in labour, one, the active contraction, probably peristaltic, of the fundus, which after labour begins gradually increases in strength, while the other is a coincidental relaxation of the cervix. When both are perfectly co-ordinated we have a so-called normal labour of average duration. If the cervical relaxation is unduly marked we find the cervix dilated, perhaps to a diameter of one and a half inches during the last month of pregnancy without uterine contractions having been felt by the patient. Such conditions are found only in multiparae, and are often followed by quick labour, indeed it may be truly precipitate. Another graph shows the typical contractions of a case of inertia. It will be noted that the contractions are irregular in both force and frequency, and that they have pointed apices, indicating a short, snappy effort, during which the uterus does not hold on to its work. It is probable that contractions of this kind are of little dilating or expulsive value, and may be associated with true spasm of the cervix. In some patients this form of irregular contraction is prolonged through labour, in others it can be quickly and entirely changed, either by the injection of pituitary extract, or by increasing the stimulus of the local uterine reflex by rupturing the membranes or pulling a leg down.

There are several factors which are known to influence the onset of labour, but it is not known which, if any, are normally responsible for the initiation of labour at term. In the lower animals the influence of the higher emotional centres can be ruled out. Chemical, hormonal, or reflex nervous mechanisms are, therefore, solely responsible. In man, however, in accordance with the general tendency of the autonomic system to abdicate its proper rule over visceral activities, we find the higher centres playing a part in proportion to the social development of the individual. While, however, the higher centres can profoundly modify the onset and course of labour, it can obviously proceed normally, and probably better, without their

interference. Similarly, when considering other factors, such as the endocrine secretions and reflex action, we find difficulties in demonstrating their universal application.

It is probable that healthy uterine muscle itself has a uniform capacity for contraction, and that variations in its action in different women, and during the same labour, are due to extraneous influences, nervous or hormonal, brought to bear on it. To elucidate the nature of the nervous control, much experimental work has been done, but the results of experiments on animals, while of interest to comparative physiologists, are of disappointing value to human physiology and clinical medicine. There are too many discrepancies and variations among the different animals to make experimental results generally applicable to women in labour. We can gain most information here, as in many other departments of medicine, by careful clinical observation. In 1871 Simpson described normal parturition in sows in which the dorsal and lumbar cord had been divided, and also described normal labour in a paraplegic woman. Still earlier, in 1867, Kehrer noted that the uterus contracted when severed from its connexions. Others have described parturition after the uterus has been extirpated from the body. Keiffer[1] described the profusion of nerve fibrils and ganglia lying along the muscle fibres of the guinea-pig, and in 1932[2] he again described the richness of the ganglion and nerve fibril supply of the uterine muscle. The ganglion cervicale of Frankenhauser generally lies in the region of the utero-sacral ligaments, but other ganglion tissue lies in the broad ligament together with pleochrome cells like those of the supra-renal glands. There is also a profuse nervous supply to the vessels of the uterus.

From these and other observations there is no doubt that the uterus is very freely supplied by nerve fibres from the sympathetic system. Beckwith Whitehouse and Featherstone,[3] by the use of spinal anaesthesia paralysed the lumbar cord, and then noted contraction of circular fibres of the fundus and cervix which they attributed to the unopposed influence of the sympathetic. We have evidence ourselves, however, that the sympathetic inhibits the contractions of the human uterus in labour. Cook,[4] by experimental work on animals, could not find any evidence of a direct nerve supply from the lower spinal cord via the nervi erigentes to the uterus and vagina. The view of modern physiologists is that a direct para-sympathetic

supply to the uterus is wanting, but presumably this opinion is based on animal experiments only.

While nerve elements are easily observed in the uterine wall, the real controversy ranges round the question of whether both the sympathetic through the hypogastric nerves and plexus, and the para-sympathetic through the nervi erigentes (sacral second and third roots) supply the human uterus in labour. Contradictory statements have been made, chiefly because observations have been made on animals, which are not applicable to man. We believe that a perfectly normal labour is largely a matter of the local myogenic contraction and local reflex activity of the uterus itself, while external stimuli such as emotion, or local stimuli such as produced by obstruction to expulsion are able, by the nervous supply, to modify the contractile activity of the uterus.

We would next mention the large group of cases of inertia due to interference of the working of the local cervical reflex mechanism. Fitzgibbon[5] has stressed the importance of the engaging and pressing head as a cause of the onset of labour, and points out the well-known fact that the pregnant woman in whom the head of the child is floating above the brim will often go over her time. Further, in a large number of patients in whom inertia is present there is some abnormality in the presentation or engagement of the head. Some labours, with the occiput posterior, are slow, but not primarily because the opposed diameter is too large, because the contractions are feeble. If the uterus acts strongly the head is flexed and rotated spontaneously. We teach too often that with the occiput posterior labour is slow because of purely mechanical reasons. It is often slow because the pressure of the head on the cervix does not arouse the cervical reflex by which the contractions are stimulated. In many cases of inertia, if careful examination is made, we find the true cause is the non-engaging or non-descending head. This view is supported by the great frequency of premature rupture of the membranes in severe cases of inertia due to the failure of the presenting part to fit well into the brim. Until it can be assured that the head is flexed, with the occiput anterior and well down on the cervix, other less defined causes of inertia need not be sought.

Dutta[6] discusses irregular uterine action illustrated by spasm, general or localized, and atony, as an inco-ordination between the longitudinal and circular muscles, or nervous, as opposed

to muscular inco-ordination. Blair-Bell[7] regards inertia as due to a lack of pressor substances, and advises calcium. Kermavner[8] discusses weak contractions in terms of the well recognized causes, such as debility, distension of the uterus or fear, but he admits that in many cases no obvious cause is clear, and does not consider that age itself is of much importance. Kermavner regards the full bladder and rectum not as causes of uterine atony, but as due to a primary condition which produces atony of all the pelvic viscera, a cause which lies in nervous control. Going still further back Kermavner is inclined to ascribe the nervous failure to lack of the appropriate sensitizing endocrine substance.

Aschner[9] ascribes the majority of labour complications to delay due to the resistance of the soft parts, and favours careful digital dilatation of the cervix, as far the best method of shortening labour in cases of slow dilatation.

Other writers, de Garis,[10] Harrar,[11] van Cauwenberghe,[12] Toneff, Kronig, and Weber discuss the relative importance of feeble contractions and cervical resistance, together with the appropriate treatment, based upon the cause of delay.

Endocrine Considerations.

A large literature has also arisen round the action of drugs on the uterus. Dale, Burn, Fleming and many others have examined this question. The discovery of the specific action of pituitary extract on the uterus gave a stimulus to the endocrine theories of labour. Also the great growth of the corpus luteum in early pregnancy, and the known power of its secretion of antagonizing the influence of oestrin on the uterus, has suggested that this gland is concerned with the continued passive growth of the uterus during pregnancy. The easy theory has been formulated that so long as the corpus luteum is active the uterus remains passive, but that when, at the end of pregnancy, the gland's influence wanes, as shown histologically by its degeneration, the uterus will become more irritable and finally pass into labour. It is clear now, however, that so much influence cannot be ascribed to the corpus luteum. One of us (A.W.B.) has recently removed both ovaries which were converted into rapidly growing lutein cysts during early pregnancy without causing abortion. Many similar cases have been reported so that we must acknowledge that the corpus luteum is not necessary for the continuance of early human pregnancy. The same theory would lead to the inference that if the corpus luteum had not

sufficiently degenerated at the end of pregnancy for its restraining influence to be removed, labour would begin and continue slowly. We have a section of corpus luteum removed during Caesarean section after 89 hours of feeble contractions, but it does not differ in general appearance of degeneration from another corpus luteum removed during a normal trial labour lasting 20 hours. We have examined a number of other corpora lutea obtained at Caesarean section, and have invariably found them degenerated. Certain experimental work on animals, and also on women, suggests that the corpus luteum is associated with the passive phase of uterine activity, but there is much evidence to show that it is not essential to the continuance of pregnancy, and that the persistence of luteal influence has no place in the cause of uterine inhibition in labour.

Oestrin. It is well known that normal labour may follow at term after removal of both ovaries of a woman during early pregnancy. As, however, Jeffcoate and others have shown that oestrin persists in the urine after removal of the ovaries, this fact prevents any accurate deductions from being drawn relating to the role played by oestrin in normal labour.

Oestrin is the only hormone connected with labour which can be estimated quantitatively, and even then it is only the excretion of oestrin in the urine which can be measured.

It has been shown by Jeffcoate[13] that there is a relative excess of oestrin over anterior pituitary hormones in the urine of women during the first stage of labour; from this it would appear that oestrin plays an important part in determining the onset of labour.

Assuming that this excess of oestrin over anterior pituitary hormones was responsible for the onset of labour, it might reasonably be supposed that injection of large amounts of oestrin into a pregnant woman would induce premature labour.

We have made attempts to induce premature labour by giving injections of trihydroxyoestrin in castor oil, 4.8 mgms. of this substance having been given to two patients at the thirty-seventh week of pregnancy. Not any effect was produced at the time, and the patients had normal labours some three weeks later. In a third case a patient, 38 weeks pregnant, was given the enormous dose of 48.00 mgms. of oestrin, divided into 10 doses over a period of 48 hours; this again had no effect, although the total dosage has been estimated by Marian as being in the region of 500,000 rat units.

In a fourth case a dose of 4.8 mgms. was given to a multiparous woman early in labour, the pains, which were feeble, did not appear to be markedly affected by the oestrin. It was interesting to note that the secretion of milk in the puerperium was not affected.

We conclude that pure oestrin, given by injection in castor oil, has no action in determining the onset of labour in the pregnant woman. In this connexion Marian, who has very kindly advised us on the experimental side of oestrin estimation, has also kindly allowed us to record some recent and unpublished work of his, in which he has failed to induce abortion in a series of pregnant mice, after injecting them with 400 units of pure trihydroxyoestrin. This is of special interest, as former workers have produced abortion by this means, but they were not using pure oestrin.

The part played by oestrin in labour is not known; Bourne and Burn claimed that it exercised a synergistic effect on the action of posterior pituitary lobe extract, on the isolated guinea-pig's uterus; doubt was cast on this work by Jeffcoate who produced an identical result with any foreign protein, and recently Marian and Newton[14] have shown that oestrin counteracts the tendency of oxytocin to produce any sort of sustained or tonic contraction of the uterus. The fact is that it is not known whether or not oestrin is an essential hormone for the process of normal labour.

In studying the subject of uterine inertia it was felt that the weak pains might possibly be due to deficiency of oestrin, and, therefore, a series of experiments was performed with the object of comparing the amount of oestrin in the urine of patients in normal labour, and in the urine of those suffering from genuine uterine inertia.

Rats from which the ovaries had been removed were used, and the technique of Allen and Doisy was followed; four injections of urine were given in 48 hours, and the vaginal smears were examined twice daily for six days following the first injection. It was found that one cubic centimetre of normal urine always produced strong heat in the rats, whereas one-tenth of a cubic centimetre of this urine was the least amount capable of producing any sort of heat.

Having established an arbitrary standard for the oestrin content of the urine of normal labour, the next step was to obtain the urine of patients suffering from genuine inertia. Owing to the rarity of true inertia, and to the fact that the urine in cases of

inertia often contain albumin, to which oestrin is adsorbed, the urine from only two patients, the subjects of genuine inertia, could be investigated. In each of these the amount of oestrin was not definitely diminished.

The only inference that can be drawn from this is that the amount of oestrin excreted in the urine of patients suffering from inertia does not differ materially from that excreted during normal labour.

Pituitary extract. One of us (A.W.B.) in conjunction with J. H. Burn, has already published some results on the use and dosage of this substance. We should like to state again that there are some cases of inertia characterized by feeble and irregular contractions in the first stage of labour, after causing much pain, which respond at once to a dose of two units of pituitary extract. We have a record of a labour showing the type of contractions in inertia, and the extraordinary action of two units of oxytocin (pitocin). The patient was a primigravida, aged 19, at term. Labour began on February 8th at 13.00 hours, and at 15.00 hours, when the os was dilated sufficiently to admit two fingers, the patient was anaesthetized with gas and oxygen, and the bag was introduced. Very feeble pains were present, and a minute dose of 12 units of oestrin, as might have been expected, did not produce any result. After 100 minutes, that is, at 17.19 hours, a dose of 2.5 units of oxytocin was given and this was followed by immediate response. The pains remained strong. The os was fully dilated for hours later, and the forceps was applied three hours later for delay, despite continued strong pains, due to a persistent occipito-posterior position. The child weighed seven pounds two ounces, and was born in good condition.

On the other hand some women, in an apparently similar condition, make no response. Considering the manifold influences which act on the uterus, this is perhaps what we should expect.

It seems now certain that pituitary extract unaided cannot induce premature labour, and even when given with other stimulating drugs, such as purges and quinine, it usually seems to have no effect. When, occasionally, there is a uterine response in the shape of recognizable painful contractions, they easily pass off in an hour or so leaving the uterus again inert.

Two other graphs are records obtained from a primigravida aged 24, five days overdue. The day before the experiment, so-called drug induction by castor oil and pituitary extract

had failed. The os, being closed, was dilated sufficiently to introduce a bougie on the end of which was a long, narrow, rubber bag. A dose of six injections of oxytocin, though producing slight contractions, failed to start labour. Four days later labour was induced by bougies.

Adrenalin definitely inhibits the human uterus in labour, by which it can be inferred that the sympathetic is an inhibitory nerve. This is a physiological point of great interest in view of the known clinical effect of fear on the course of labour. Whitehouse and Featherstone state that the sympathetic stimulates the circular muscle of the corpus and cervix, but we think their method of lumbar anaesthesia, whereby a number of nerve roots, including origins of both sympathetic and parasympathetic, would be thrown out of action, was not sufficiently refined to allow of positive conclusions. A graph (Bourne and Burn) shows that there is no increase in intra-uterine pressure after injection of adrenalin.

The Condition of the Cervix in Labour.

In any given case of delay in labour in which the mechanical conditions are normal, it is not always possible to state how much of the delay is due to the weakness of uterine contractions, and how much to resistance of the cervix to dilatation. Should the contractions of the uterus be of normal strength the problem of inertia does not properly arise, even though labour may be greatly delayed by non-dilatation, but in practice it is not easy always to separate the groups and, therefore, we propose to consider the possibility of true fibrous rigidity as opposed to muscular spasm of the cervix, which is part of an imperfect uterine co-ordination.

In an attempt to obtain some facts bearing on this question, we have obtained specimens of the cervix at the time of delivery, and examined them microscopically for evidence of an unusual amount of fibrous tissue, or lack of muscular tissue.

Two sections, stained by van Gieson's method, were obtained from cases of normal labour.

Case I.—A young primigravida in whom labour was normal. The section shows slightly oedematous tissue with engorged vessels, and a few small ovula Nabothi. There is a considerable amount of muscle tissue, lying in bundles, with no disproportionate amount of fibrous tissue.

Case II.—A primigravida, aged 30, in whom the first stage of labour was 12 hours, and delivery with the forceps, for delay, in the second stage. Uterine contractions were normal. The cervix shows some muscle tissue, much congestion and extravasion of blood.

Six sections of cervices were obtained from cases of inertia:

CASE III.—Mrs. D. was the subject of prolonged inertia of the uterus. An occipito-posterior position was rotated manually. The membranes ruptured after 31 hours of feeble contractions. After 77 hours the os admitted two fingers, and a pair of long, straight, narrow-bladed forceps was applied, and a weight of one pound attached. At 86 hours the head of the child was well down. At 103 hours the cervix was fully dilated and a live baby of nine pounds was delivered.

The section shows oedema, haemorrhage and inflammation, indicated by polymorphonuclear and plasma cells. There are recognizable muscle fibres, but they seem to be less than in the normal cervices.

CASE IV.—Mrs. M., aged 25, a primipara. After 56 hours the os was only half dilated, but not oedematous. The contractions were infrequent and feeble, but painful. The section shows a little muscle tissue.

CASE V.—Mrs., L., aged 26, primigravida. The presentation was a second vertex, the head was well flexed. The os was only half dilated after 72 hours. Feeble and painful contractions were present. There was a moderate caput succedenaeum and slight oedema of the cervical lip.

The section of the cervix shows fibrous tissue, denser in relation to blood-vessels. Muscle tissue is absent. The whole section is uniformly infiltrated with polymorphs, and histiocytes, sufficient to suggest a sub-acute inflammation.

CASE VI.—Mrs. O'D., primigravida, aged 26. On admission the os admitted one finger after 36 hours of feeble labour. Pains for 12 hours were absent when the membranes ruptured and the pains were good for five hours. The os remained at the same stage of dilatation. For the next 24 hours the pains were weak and infrequent. By this time, 72 hours after labour began, the patient was definitely infected (temperature 103, pulse-rate 120). The cervix admitted two fingers, was thick and fleshy, the head was well down. Doses of atropin gr. 1/100 at 3.0 p.m. and 5.0 p.m. did not have any effect on the cervix. The administration of chloroform, given as capsules, for two hours also did not have any effect. After 96 hours perforation was performed, the os admitting three fingers. Delivery was effected by weight-traction 12 hours later. The cervix was not torn and there was not any haemorrhage. The patient died four hours later of infection. The uterus had developed a mild contraction ring at the time of perforation. The section of the cervix shows a normal amount of muscle tissue.

CASE VII.—A section kindly lent to us by the pathologist of the London Hospital, taken from a cervix which was torn circumferentially around the os, and discharged in front of the child's head, after great delay in the first stage of labour. The section shows a mass of fibrous tissue and extravasated blood, but not any muscle tissue.

CASE VIII.—A section from a similar case of circumferential tear, now in the museum of St. Mary's Hospital, was kindly supplied by the pathologist, Dr. Newcomb. The section also shows a mass of fibrous tissue without muscle fibres.

Consideration of these sections provides evidence that in some cases of delay the cervix has a preponderance of fibrous tissue, and in some muscle tissue cannot be seen. The term "rigid" applied to the cervix strictly means a condition of fibrotic inelasticity, and it is clear that in a few cases the term can be properly used. The clinical counterpart of fibrosis is probably very prolonged delay, deep spontaneous tears, or even circumferential avulsion. It is to be remembered, however, that some of our cases have had feeble pains in addition to fibrosis, while the two with circumferential tears had very strong contractions. In the vast majority of cases it is true that delayed dilatation with good contractions is due to spasm of the cervix, and not fibrosis.

Mathieu and Schauffler[15] state that true primary cervical dystocia is always due to fibrosis, and not due to nervous incoordination, but they recognize that there are other forms of non-dilatability, though the action of atropin is disappointing.

Loiseauz[16] regards the non-dilating cervix as the chief factor in dystocia, and recognizes disease of the cervix, together with hindrances to dilatation by nervous influences, of which the latter is the commoner.

Treatment.

As we have already suggested, we consider that we have a definite prophylaxis for some cases of inertia in the treatment of fear during pregnancy. We have noted the strong inhibitory effect of adrenalin on uterine activity, and we know that liberation of adrenalin is associated with states of fear. Many women, especially in their first and second pregnancies, are afraid of the forthcoming ordeal of labour to such an extent that it absorbs their thoughts, to the exclusion of the ordinary affairs of life. We can see this in the anxiety some pregnant women show about every little detail of their physical welfare. Nothing is taken for granted, and the smallest symptom, or pain, is regarded as a portent of mischief. A suggestion that anything whatever is not perfectly normal fills them with terror. These women pass through pregnancy and approach labour suspicious that the abnormal is probable, while the contented, care-free woman goes along with gladness, and assumes that the normal is the only and obvious condition. Most of us can foretell that the first woman will have a long and tedious labour with the maximum pain, while the second will begin labour well and pass through quickly and spontaneously. We think that fear has a large part to play in causing weak contractions. It

is a feature of the more civilized levels of society in which slow labours are most often seen, while in hospital practice, in which women take labour as a matter of course, we see much less trouble caused by inertia.

Most medical men will admit that the frightened woman will have a "bad time," yet it is not sufficiently realized what a large part fear plays and, therefore, how important it is to prepare the woman's mind during pregnancy by constant encouragement and development of confidence at the antenatal visits. In fact when, as in the majority, there is nothing organically wrong, the chief object of the antenatal visit is the opportunity it gives for communicating a feeling of faith and confidence.

Our paper should, strictly, deal only with those cases of protracted labour due to feeble expulsive power, but in a clinical account of the subject it is not easy to separate the true cases of inertia from those less common cases in which there is a combined non-dilatability of the os. We shall therefore include the latter type in our discussion on treatment.

After labour has started, its mode of onset, and the physical condition of the presenting part, will be a guide to treatment. If labour begins slowly, with anxiety and exaggerated response to the contractions, morphia and scopolamine should be given as soon as possible. The latter should be repeated from time to time when necessary.

When the presentation and pelvis are normal the best of all treatments is the old method of giving sedatives in the form of morphia, scopolamine, chloral and bromide. In some patients, nembutal with chloral has proved a valuable method. So long as the membranes are intact further treatment need not be contemplated unless it be by rupturing the membranes artificially, which may be safely done when the os is three parts or more dilated, and especially in multiparae. The excitation of the local reflex is brought into action, and is usually effective in stimulating contractions.

Treatment on the opposite lines is to attempt to increase the strength of the uterine contractions. The chief method is by the use of pituitary extract, but so far this treatment has not gained much popularity. We are convinced, however, of its value in selected cases, and one of us (A.W.B.) in conjunction with J. H. Burn, has published evidence that small doses of pituitary extract (not more than two and a half units) given during the first stage of labour will often alter the character of contractions

from that of inertia to a normally progressing labour. Pituitary extract does not succeed in all cases, however, and care should be taken that mechanical difficulties are not present. In any case a dose of two and a half units cannot do any harm.

It is well known that the great majority of patients suffering from inertia can safely be treated by sedative drugs and patience. The mistake usually made is to interfere actively too soon, and the chief difficulty is to know when to adopt such measures. There comes a time during labour when a patient suffering from long drawn-out inertia when a fine obstetric judgment can recognize that the further administration of sedatives and waiting are useless, a point of time from which both mother and baby will begin to deteriorate unless some active treatment is adopted.

If, therefore, it is decided that the time has come to act, the first thing to be done is to explore the dilatability of the os under anaesthesia. The os is usually found much softer and more dilatable than was expected, or rarely it may have a thick unyielding edge. The head of the child will nearly always be found unrotated, and in all cases verification of the anterior position should be made. If the os is soft and dilatable, it should be gently opened up by the fingers to its greatest extent, and then pushed up over the head, beginning posteriorly. This is more easily done if the forceps is applied, and the os pushed up over the child's head as it is held or gently pulled down. There is generally little difficulty in this manœuvre, but however careful one may be, the cervix is usually found to be quite deeply torn after delivery.

The difficulties and grave dangers arise in those patients in whom the os is not dilatable. We have now a choice of method depending on the condition of mother and baby. If both are good, and ordinary possibilities of infection can be ruled out, there is a limited number of patients for whom lower segment Caesarean section can be performed. This is especially advisable if we are dealing with a primigravida over 40 years of age in whom we may expect extensive and dangerous tearing of the cervix and when, also, the baby may be the only one she is likely to have.

Published results of Greene-Armytage,[17] and Danford and Grier[18] clearly indicate that this is a safe operation. We believe that the risk is definitely less than that attending manual or incisional dilatation of the cervix and craniotomy at a much later stage when the mother is exhausted and heavily infected.

If the case is first seen at a later stage when the child is dead and the mother's condition demands delivery as soon as possible, we recommend manual dilatation of the cervix, slowly and carefully, so far as possible, followed by perforation and attachment of the cranioclast. If the os is still not more than half dilated we attach a weight of four or five pounds on to the cranioclast, so using continuous traction. By this method there is less chance of tearing the cervix, and less shock caused, than by rapid delivery.

An alternative method recommended by some writers is to make two postero-lateral incisions in the cervix. We regard this practice as essentially dangerous in so much as the incisions are likely to be extended by deep tearing, and since these cases are often dangerously infected at this last stage, the risk of septicaemia is definitely increased. If continuous traction fails after a fair trial of three or four hours, treatment by multiple small incisions of the cervix become necessary.

As soon as the placenta has been delivered the uterus should be injected with six ounces of glycerine and iodine, two per cent, as a prophylaxis against puerperal sepsis.

Conclusions.

1. Uterine inertia is probably one of the chief indirect causes of obstetric disasters.

2. Inertia is probably an inco-ordinated uterine peristalsis, in which not only is the contraction weak, but there is failure of the cervix to relax.

3. The factors which influence the strength of the contractions include nervous inhibition by the sympathetic, the proper working of the local cervical reflex, and possibly endocrine secretions.

4. Of the endocrine influences we know for certain the stimulant action of pituitary extract, and the inhibitory action of adrenalin. Oestrin in massive dose (48.00 mgms.) has failed to induce uterine contractions at the thirty-sixth week. It has probably not any effect on the initiation or course of labour, There is not any discoverable difference in the oestrin-content of the urine in normal and delayed labour.

5. The histology of the cervix in labour shows some cases of fibrosis and absence of muscle fibres, particularly in two cases of circumferential tear of the cervix. In the cervices of women who have had normal labour, muscle bundles can be clearly seen.

6. A clinical summary and tables have been given.

7. The treatment of the majority of cases of inertia is by the expectant use of sedative drugs. The chief danger lies in too early interference which results in lacerations, shock, haemorrhage and sepsis.

8. The preliminary to active interference is to examine the manual dilatability of the cervix under anaesthesia, and ascertain the exact position of the head.

The majority of cervices are easily dilatable. The cervix should be pushed up over the head and slow delivery completed by the forceps.

10. If the cervix is not dilatable, but all other conditions are good, lower segment Caesarean section may be performed.

11. If the child is dead, its head should be perforated and a cranioclast then affixed, and the child should be delivered by continuous weight traction.

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(*The discussion on this article will be found on page* 535.)

The Histological Classification of Cancers of the Uterine Cervix, and the relation between Cellular Structure and Prognosis after Radium treatment.

BY

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FROM the time that it was recognized that a cancer consisted of a mass of cells, and that its malignant nature was dependent upon the abnormal behaviour of those cells, numerous attempts have been made to correlate the minute anatomy of a cancer and its clinical manifestations. Such studies received a fresh stimulus with the advent of radiation therapy in the early years of the present century. Malignant growths which appeared similar to the naked eye, were noted to vary enormously in their reaction to the rays, and a histological explanation was sought for this variation in response.

That there is a relation between the structure of a cancer cell and its behaviour was first suggested by Hansemann[1] in 1893. He introduced the term "anaplasia" for lack of differentiation, and he believed that there was a direct relation between anaplasia and the invasive capacity of a growth. Afterwards, little progress seems to have been made in this aspect of cancer cytology until 1920, when Broders in a study of carcinomata of the lip,[2] and later of the skin,[3] and genito-urinary organs,[4] found that the likelihood of cure following operation depended to a great extent upon the microscopic appearance of the tumour concerned. Broders divided epitheliomata into four groups, according to the degree of differentiation they showed towards normal squamous epithelium, and he observed that the outlook after surgical excision improved with the maturity of the cancer.

Since then many investigators have tried to base the prognosis of carcinomata on the histological picture, but the results of

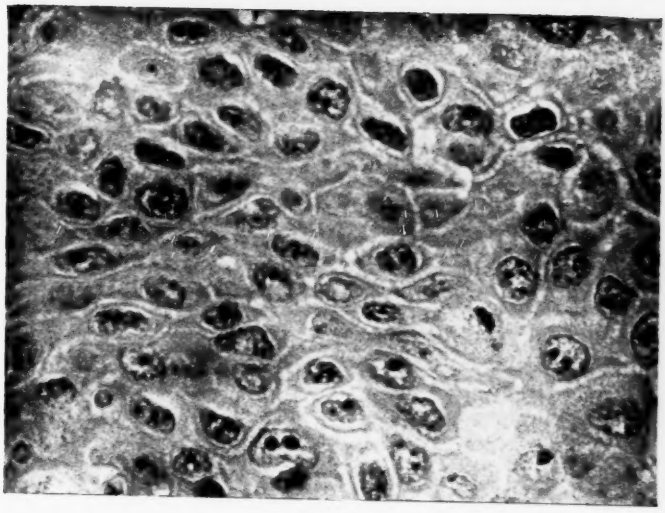

FIG. 1.
Spinal cancer cells. × 500.

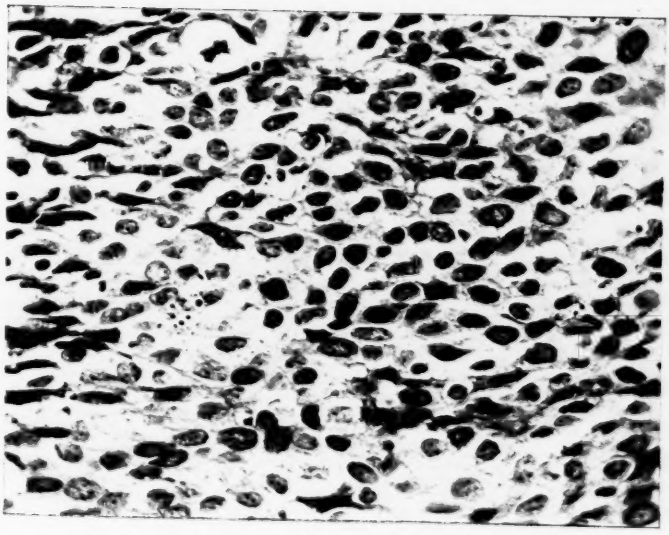

FIG. 2.
Transitional cancer cells. × 500.

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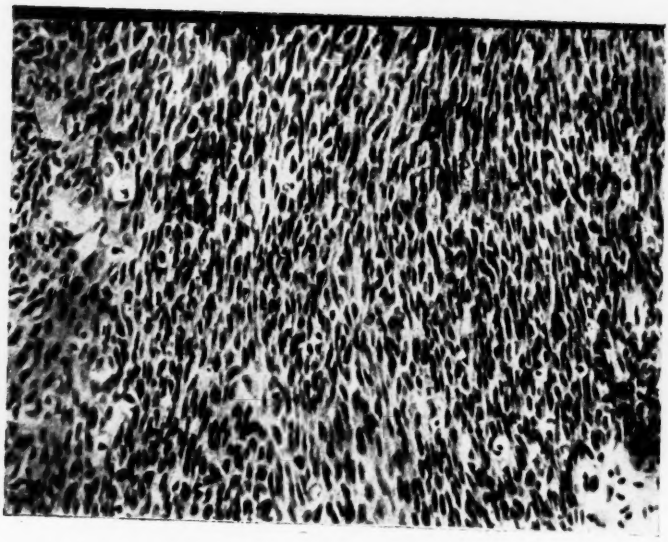

FIG. 3.
Spindle cancer cells. × 250.

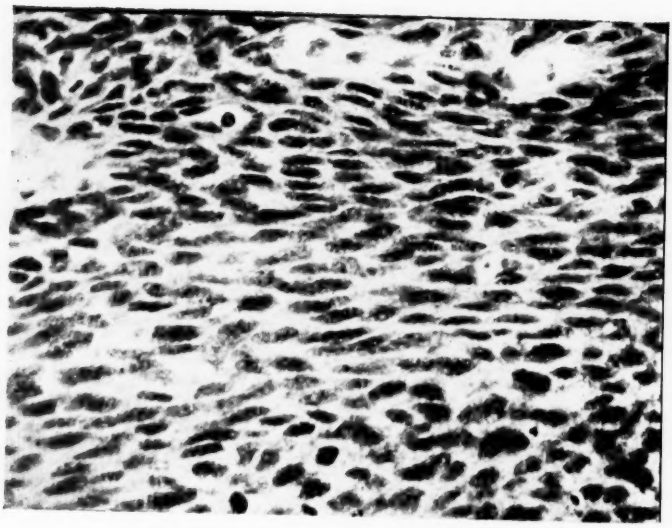

FIG. 4.
Spindle cancer cells. × 550.

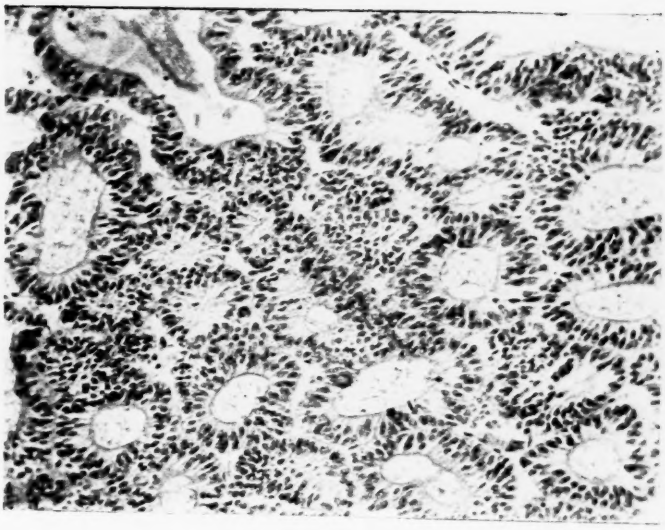

FIG. 5.
Adenocarcinoma. × 150.

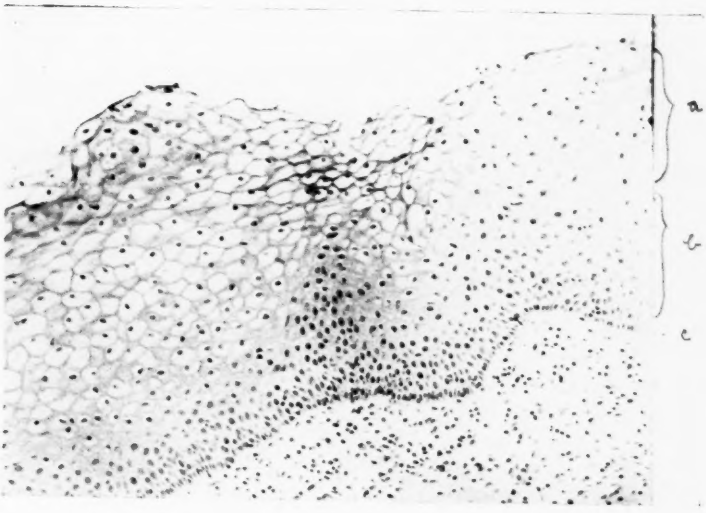

FIG. 6.
Normal stratified cervical epithelium. × 130.

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such studies have not been uniform. This lack of agreement is partly accounted for by the absence of a standard method of classifying cancers histologically, and until some uniform method of microscopic grading is generally adopted, the pathological material and diagnosis at different clinics will hardly be comparable. A certain amount of confusion has also entered the problem through attempts being made to compare results obtained by different therapeutic methods. The form of treatment used, whether surgical or radiological, is of the first importance when trying to correlate structure and result.

This investigation was undertaken to study the possibilites, and some of the difficulties, associated with the various methods of classifying cancers of the uterine cervix on a microscopic basis, and then to examine the bearing of such a histological study on the prognosis after radium treatment.

For this purpose a review was made of the microscopic slides belonging to a series of 236 cases of cancer of the uterine cervix which had been admitted to the gynaecological wards of the Cardiff Royal Infirmary during the last 10 years. Some of the more recent cases only have been under my care, the large majority having been treated either by Sir Ewen Maclean or by Professor Strachan, both of whom have kindly placed their records and pathological material at my disposal. The cases have been taken consecutively, only those few omitted in which the biopsy material was either insufficient or unsuitable for reliable microscopic grading owing to superadded inflammatory or degenerative change.

The first question to be considered was whether it was possible to classify cervical cancers satisfactorily, and consistently, into more than the two groups of solid cancers and glandular cancers. Owing to the wide variation of microscopic detail displayed by the solid cancers of the cervix, many investigators have tried to grade them according to their histological structure.

The basis of most of these classifications has been the degree of anaplasia or de-differentiation exhibited by the growth. Schottlaender and Kermauner,[5] in 1912, were among the first to classify cervical cancers in this way. These authors grouped them into mature, half mature and immature types. Other investigators have classified them into adult, plexiform and anaplastic types,[6] or into ripe, mid ripe and unripe types.[7] Martzloff's method of classification also depends upon the degree of differentiation, but the grading is based solely upon the microscopic appearance of the individual cells of which the main mass

of the neoplasm is composed.[5] Classifications which take into account the regularity or irregularity of the histological pattern, and the amount and character of the stroma, may be of more prognostic significance to the observer, but such methods are influenced too much by the individual histologist to be of any comparative value. It is partly for this reason that in this paper Martzloff has been followed, and something definite such as cell structure has been taken as the basis of the grouping.

Ten of the 236 cases (4.26 per cent) were glandular cancers. They were of a fairly uniform microscopic appearance, and were too few to make worth while any grading into differentiated and undifferentiated types.

The remaining 226 cases were solid or epidermoid cancers, and in these it was possible to recognize three fairly distinct types of cancer cell, which have been named by Martzloff[8] the spinal, transitional and spindle cancer cells.

The spinal cancer cells (Fig. 1) resemble to some extent the cells seen in the superficial zone of normal stratified cervical epithelium. The cells are adult in character and show squamous tendencies with occasional cell-nest formation. The cells are polyhedral in shape and have well defined cell membranes. The cells contain large nuclei, which stain moderately with haematoxylin, and abundant cytoplasm which takes on a light eosin stain. As their name suggests, these cells are the homologues of the prickle cells, but although they resemble the prickle cells in shape, the intercellular protoplasmic bridges, or prickles, are not always easy to find.

The transitional cancer cells (Fig. 2) are by far the most common variety. They resemble in appearance the cells found in the middle layers of stratified cervical epithelium, and it was for this reason that they were called by Martzloff the transitional cell type. They do not have any characteristic shape, but tend to be round. Squamous characters are slight, or absent, and prickles are not seen. They also differ from spinal cells in containing a relatively small amount of cytoplasm, and in having faint outlines. Moreover, the nucleus and cytoplasm stain more deeply with haematoxylin and eosin.

The spindle cancer cells (Figs. 3 and 4) are smaller cells and are, as their name suggests, spindle shaped. Their nuclei take a deep haematoxylin stain, and, since there is only a small amount of cytoplasm in the cells, the nuclei are closely apposed. Some parts of the field may almost look like a sarcoma.

The chief characteristics of the three types of cell are shown in tabular form below:

	Spinal	Transitional	Spindle
Shape	polyhedral	usually round	spindle
Cell membrane	well defined	faint	faint
Nucleus stains with haematoxylin ...	moderately	well	deeply
Cytoplasm amount	abundant	less abundant	scanty
Stains with eosin	pale	well	well

At this stage is is interesting to note that some gynaecologists believe that the microscopic structure of a solid cervical cancer depends upon the layer of the cervical integument from which it has arisen. The stratified squamous epithelium of the portio vaginalis, like similar epithelium elsewhere, can be differentiated into three layers (Fig. 6). The superficial stratum (Fig. 6a) is composed of partly flattened cells with well marked cell membranes. These cells contain a moderate amount of cytoplasm, which stains only faintly with eosin. The intermediate stratum (Fig. 6b) is composed of smaller cells which contain less cytoplasm, and have outlines which are less distinct than those of the superficial layers. In addition their nuclei and cytoplasm stain more deeply with haematoxylin and eosin. Finally there is usually a single, but occasionally double, layer of deeply staining cells arranged with their long diameters at right angles to the surface of the epithelium, known as the stratum germinativum (Fig. 6c).

It has been suggested that the spindle cell cancers originate in the basal layers of this stratified cervical epithelum, and that the transitional and spinal cell cancers arise from cells more superficially placed, whereas, if the columnar cell epithelium of the cervical canal is the seat of malignancy, the result is an adenocarcinoma. However, epidermoid cancers occur both in the portio vaginalis and in the cervical canal, and such growths are occasionally seen in the body of the uterus. In view of the well known tendency of malignant epithelial cells to change their form,[9] it does not seem possible to obtain reliable information concerning the histogenesis of a cancer merely from its cellular structure. This point has been referred to only in order to stress the fact that the classification adopted in this paper is a purely morphological one, and is not meant to carry any histogenetic implications.

The majority of the solid cancers were found to be composed of all three types of cell, and only 21 per cent of the growths consisted solely of one cell type, 9.7 per cent of the spinal cell cancers and 11.5 per cent of the transitional cell cancers were pure cell forms. Pure spindle cell growths were not found. The usual finding was, therefore, a mixed cell growth, and in such cases the classification was made upon the predominant type of cancer cell present. Classifying the growths in this way 30.9 per cent were found to belong to the highly differentiated spinal cell group. At the other extreme there was a smaller group comprising 13.3 per cent of the cases, in which the tumour was composed of closely packed spindle and polyhedral cells. In the spindle cell growths a considerable admixture of small round and polyhedral cells was always found. Between these two groups there was a large intermediate group in which the tumours were composed mainly of transitional cells and showed moderate anaplasia. 55.8 per cent of the cases fell into this transitional cell group. This class is large because there is a tendency for it to receive all cell types which are not typically spinal or spindle in character. Though the occurrence of cornification could usely be taken as evidence of a mature cancer, pearls were occasionally seen in immature growths.

The incidence of the different cellular types of cervical cancer found in this series is shown in Table I.

TABLE I.

The distribution of cell types in 226 epidermoid cancers of the uterine cervix.

Cell type	Number of cases	Per cent	
Spinal cells with cornification ..	13	5.8	
Pure spinal cells	9	3.9	30.9 per cent
Spinal with transitional cells ...	48	21.2	
Transitional with spinal cells ...	70	31.0	
Pure transitional cells	26	11.5	55.8 per cent
Transitional with spindle cells ...	30	13.3	
Spindle with transitional cells ..	30	13.3	13.3 per cent
	226		
Adenocarcinoma	10	(4.2 per cent of 236 cases of cervical cancer)	

It was not difficult to place a large proportion of the tumours into one of the above groups, but it soon became apparent that

there were difficulties associated with any classification based upon the microscopic appearance of the tumour cell.

Perhaps the greatest obstacle to a satisfactory grouping was the multiplicity of cell types found. Certain cells were definitely of the spinal type, and others were just as definitely of the transitional or spindle types but, from typical spinal to typical transitional cells, every graduation of cell was seen. Difficulty was not experienced in distinguishing between a spinal and spindle cancer cell, but it was not always easy to decide the appropriate grouping of a transitional cell tumour which bordered upon, and had some of the characteristics of, one of the other groups. The most unsatisfactory tumour cells to classify were certain of those which were intermediate between the spinal and transitional types. Such a cell was one which possessed most of the characteristics of a spinal cell, but had an indefinable cell membrane, or on the other hand, a cell which had the deeply staining nucleus of a transitional cancer cell but had a particularly well-marked cell outline. These are the types which may be differently interpreted by different observers. In this series the former were included in the spinal group, and the latter in the transitional cell group. It is important to recognize that in degenerated areas of growth, the outlines of transitional cells can be more clearly made out owing to their distension.

The personal factor may also enter the classification of certain growths in which no cell type is present in striking preponderance. In such a case there may be a difference of opinion with regard to the relative proportions of the different types of cell present, but in almost all cases, if there is sufficient pathological material available, the predominant type of cell can be determined. In the majority of cases, several sections taken from the vaginal aspect of the growth were available for examination, and though minor variations in structure were observed, the distribution of cells throughout the tumour was usually found to be fairly uniform. The sections were taken from the growing margin of the tumour before it was exposed to radium. Though the recurrence of a cancer after radium generally had a structure similar to that of the original growth, there was sometimes a tendency for it to show a more adult or differentiated appearance.

The operation of the personal equation is evident to a certain extent in Table II, in which the incidence of the four types of cervical cancer in this series is shown in comparison with those found by Martzloff[8] and Pemberton[10] using a similar method of grouping.

TABLE II.
Percentage distribution.

	Cardiff	Martzloff	Pemberton
Number of cases investigated ...	236	387	96
Cell type			
Spinal	29.6	15.5	30
Transitional	53.5	66.8	56
Spindle	12.7	12.3	6
Adenocarcinoma	4.2	5.4	8
Pure cell types			
Spinal	9.7	3.6	6.2
Transitional	11.5	21.4	9.3
Spindle	0.0	4.6	0.0
Total ...	21.2	29.6	15.5

THE PROGNOSIS IN CANCER OF THE UTERINE CERVIX.

The prognosis in any case of malignant disease is governed by several factors, and in order to be able to examine the influence of any one of them, in this instance histological structure, it is necessary to control, so far as possible, the effect of the remainder.

In cancer of the cervix, the final result depends upon the malignancy of the tumour, its extent when treatment is begun, and the form of treatment adopted. Under radiation treatment, a fourth variant is introduced, namely, the susceptibility of the growth to radium. If the histological structure of a cancer affects the prognosis in any way after radiotherapy, it must do so in virtue of its relation to one or both of the properties intrinsic to the tumour itself, namely, its invasive capacity and its radiosensitivity.

The influence of any single factor can be estimated with less difficulty in this group of cases owing to the fact that they have all been treated with radium by a fairly uniform technique, the dosage varying only slightly according to the condition found in any individual case. The method used has already been described by Professor Strachan.[11] As for the clinical extent of the disease, it is now fully established that this is one of the most important factors governing the permanency of cure, and its influence will have to be carefully controlled throughout. In order to ascertain whether the prognosis was affected by other factors of similar importance, the relation of such variables as the age and general condition of the patient, and the naked eye character of the growth, to the three-year survival rate was examined. Without presenting the figures relating to this portion

of the investigation, it may be said that of all the factors examined, the only one which had any appreciable influence on the final result was the gross extent of the disease, and since the treatment was fairly uniform, this is the only factor the influence of which has to be controlled.

The prognostic significance of histology can now be studied by comparing the results obtained with radium in the four structural groups.

The Response to Radium Treatment in the Four Structural Groups.

The response to radium treatment has been examined from two aspects, by noting first the immediate attempt of the ulcer at healing, and secondly the condition of the patient three years later.

The immediate response. The condition of the ulcer three months after irradiation has been taken as a criterion of its immediate reaction to treatment, and 100 advanced cases (Stage 3 growths) have been examined from this point of view. One quarter of the ulcers had healed, and Table IIA shows the tendency towards healing in the four structural groups.

Table IIA.

The immediate response to radium treatment in 100 advanced cases of cervical cancer, grouped according to the predominant type of cell.

Cell type	Number of cases	Number locally healed within three months of treatment	Per cent
Spinal cells	36	9	25
Transitional cells	56	13	23
Spindle cells	4	2	50
Adenocarcinoma	4	1	25
	100	25	25

The histological type which showed the best immediate response to radium treatment was the spindle cell cancer. If it is permissible to take this immediate response as an index to the radiosensitiveness of the growth, we may conclude that the spindle cell cancers were the most susceptible to radium, and the radiosensitivity of the three other histological types was approximately equal. This would be in accordance with the Law of the Radiation Sensitiveness of Tissues of Bergonie and

Tribondeau which reads, "Immature cells and cells in an active state of division are more sensitive to rays than are cells which have already acquired their fixed adult and physiological characters."

Though it is clear to the most casual observer that cancers of the cervix vary considerably in their clinical reaction to rays, the qualities which determine this variation in response are still unknown. The general condition of the patient, and the degree of infection in the region of the ulcer, are probably of importance. So far attempts to correlate radiosensitiveness and histological structure have proved inconclusive. Some (Alter,[12] Schmitz,[13] Healy and Cutler,[6] Ewing,[14] Cordua[15]), believe that the unripe types are the more radiosensitive, whereas, others (Regaud,[16] Adler,[17] Lahm[18]), have come to opposite conclusions. On the other hand, some assert that the cell type does not bear any relation to the radiosensitiveness of the tumour and that the stroma is of more importance. Cramer[19] observed better results in cancers with a hyperaemic stroma, than in those in which the stroma was anaemic, while Pemberton[10] found that tumours containing more stroma than cancer tissue responded better to rays.

Though there is still a considerable divergence of opinion on the question, the mass of evidence suggests that the more undifferentiated a cervical cancer is, the greater is its radiosensitivity. Our findings point in the same direction, but the figures are too small to allow deductions to be made with confidence. Nevertheless, this view receives a considerable measure of support from the behaviour of certain carcinomata in other parts of the body. One of the most radiosensitive of all growths is a highly cellular anaplastic type of cancer seen in the base of the tongue and tonsillar region. It is so radiosensitive that this feature alone has become a point of differentiation between it and the more radioresisant squamous cell carcinoma found in the same situations.[20, 21] Such highly sensitive cancers are not seen in the uterine cervix, but on grounds of analogy the more anaplastic spindle cell cervical cancers would also be expected to react the more favourably to the rays.

The Three-year Survival Rate.

The more permanent results have been examined in a group of 151 women treated more than three years ago, and they have been estimated on the basis of the three-year survival rate, and also on the length of life after treatment. The former are not so

acceptable a standard as the five-year survival rate, but the third and fourth years cases have been included in order to increase the number of cases available for study, and so make the analysis a little more accurate statistically. Attempts to establish a connexion between the histological type of a cancer and its prognosis after radiological treatment have produced results which show little agreement. According to Healy and Cutler,[6] Boehm and Zweifel,[22] Alter,[12] Schmitz,[13] among others, the best results are obtained in the rare anaplastic tumours. Pemberton,[19] and Pomeroy and Strauss,[23] on the other hand, found the outlook better in the spinal or rare adult cancers. Kimbrough and Norris[24] also had slightly better results in the prickle cell cancers, but the differences in their cases were so small that they concluded that the microscopic appearance was not of any prognostic value after radiation.

Table III shows the three-year survival rates in the four structural groups. The cases have been divided into early and advanced groups in order to control so far as possible the influence which the gross extent of the disease is known to have upon the final result.

TABLE III.

The three-year survival rates in the four structural groups.

Cell type	Early cases (stages one and two) Number of cases treated	Early cases (stages one and two) Three-year survival rate per cent	Advanced cases (stages three and four) Number of cases treated	Advanced cases (stages three and four) Three-year survival rate per cent	Total Three-year survival rate per cent
Spinal cells	7	28.6	30	10.0	13.5
Transitional cells ...	20	30.0	66	6.0	11.6
Spindle cells	5	40.0	16	12.5	19.0
Adenocarcinoma ...	2	50.0	5	20.0	28.6
Total ...	34	32.4	117	8.5	14.0

The figures show, rather surprisingly, that better results have been obtained in the glandular cancers than in the epidermoid cancers, and that of the latter the spindle cell growths responded best to treatment.

Table IV shows the relation between histological structure and the duration of life after treatment, in 100 fatal and non-fatal advanced (Stage 3) cases treated more than three years ago, and grouped according to their cellular types.

TABLE IV.

Cell type	Average duration of life after the first application of radium
Spinal cells	10.8 months
Transitional cells	14.2 ,,
Spindle cells	14.8 ,,
Adenocarcinoma	45.0 ,,
For whole group ...	14.6 months

These figures support the same conclusions. However, figures which may appear convincing when arranged in one way may change their whole meaning after, perhaps, a slight alteration in the manner in which the material is grouped. So in order to gain further information on the relation between cellular structure and prognosis, the distribution of cell types was analysed in the following groups of patients, (Table V) in one group of women who had progressed satisfactorily, and in two other groups of women who had responded to treatment particularly badly.

TABLE V.

Cell types	Percentage distribution of cell types in 20 patients who have survived for three years	236 unselected cases	27 fatal stage two cases	56 patients who died within six months of treatment
Spinal cells ...	20	29.6	22.2	26.8
Transitional cells ...	50	53.5	63.0	58.9
Spindle cells ...	20	12.7	11.1	10.7
Adenocarcinoma ...	10	4.2	3.7	3.6

These figures show that in spite of the widest divergence in clinical results, the differences in the distribution of the cell types in the various groups are only slight. However, the small differences present support the previous conclusion that in this series of cases the adenocarcinomata and the spindle cell cancers have given the slightly better results.

This is most interesting in the case of the adenocarcinomata. In the experience of most gynaecologists the glandular cancers have proved almost entirely refractory to radiotherapy. Thus in 1916 Adler[17] recorded 14 cases of adenocarcinoma of the cervix and vagina treated by radiation in which only three showed any improvement. In 1930 Keller reported that of 310 cases of cervical cancer admitted to the Freiburg Hospital for Women five were adenocarcinomata. In spite of the fact that four of

the five cases were operable not any patient lived for more than 25 months after radiotherapy, and the average duration of life was 15.4 months.

Seven of the 151 cases in this series were adenocarcinomata. Two of the women are still alive, having been treated six and four years ago respectively, whereas the average duration of life after treatment in the five fatal cases was two and a half years.

In view of these results it is interesting to note that Wintz[26] disputes the interpretation that adenocarcinomata of the cervix are unsuitable for radiation therapy, and concludes that though their radiosensitivity is a little less than that of the squamous epitheliomata they can still be cured by radiological methods. Healy and Cutler[6] also found that cervical adenocarcinomata were not particularly radioresistant, and that the outlook was as good as it was with epidermoid cancers. Pomeroy and Strauss[23] obtained their best results with radium in the case of spinal cell cancers and adenocarcinomata.

Discussion.

Many circumstances influence the prognosis in cervical cancer after radium treatment, and the object of this investigation has been an endeavour to ascertain whether the cellular structure of the growth plays any part in the final result.

As previously mentioned, if the histological structure of a tumour affects the prognosis after radium treatment it does so in virtue of its relation either to its malignancy or to its radiosensitivity.

The bearing which the histological structure of a growth has on its susceptibility to radium has been considered, and although there is no unanimity upon the question, the radiosensitiveness of a tumour usually seems to be inversely proportional to its degree of differentiation.

Broders,[2,3,4] Martzloff[8] and others consider that the predominant type of cell present in a cancer also indicates with a fair degree of accuracy the relative malignancy of the tumour. Broders,[2] in his study of epitheliomata of the lip, came to the conclusion that the more a growth differentiates the lower is its degree of malignancy. He pointed out that the life history of any cell consists of two processes, reproduction on the one hand, and differentiation and specialization on the other, and in any one cell the activities of these two processes seem to be inversely proportional. The more a cell differentiates the less is

its power of reproduction, and in the case of a malignant cell the less is its degree of malignancy. So when tumours are classified according to their differentiated characters, they are also, in the light of this biological law, being graded to some extent according to their reproductive abilities. It would, therefore, be expected that the more mature spinal cell cancers of the cervix would be less malignant that the transitional cell cancers, and the latter in turn as less malignant than the spindle cell growths, and these deductions are supported by the results of hysterectomy.[4, 27] It is the tumour with undifferentiated cells which are usually fast-growing and malignant and which, according to Broders,[3] Martzloff,[8, 27] Pemberton,[10] Pomeroy and Strauss[23] and others give a particularly bad prognosis after surgical excision. These investigators agree that hysterectomy obtains its best results in the alult types of cervical cancer. Conflicting opinions have been expressed as to the malignancy of adenocarcinomata. Lynch[28] considers them to be more malignant than the epidermoid cancers, whereas Martzloff found their malignancy to be intermediate between that of the spinal and transitional cell types.

If radium acted to the same extent upon all cancers, radiotherapy would probably resemble surgery in obtaining its best results in the less malignant growths. On the contrary, in this series the spindle cell cancers, though apparently the most malignant type, gave as good if not a little better results than the more benign spinal cell growths. This experience of obtaining the best results in the more malignant growths would be difficult to understand unless the influence of some additional factor had been introduced, and this variant seems to have been the radiosensitiveness of the tumour. Since the most malignant growths appear to be also the most susceptible to radium, and vice versa, the balancing of these two factors seems to have produced practically equal results in the four structural groups. In fact, the high degree of malignancy of the spindle cell cancers appears to have been more than offset by their greater radiosensitiveness.

Summary and Conclusions.

The relation between cellular structure and response to radium treatment has been studied in a series of 236 cases of cancer of the uterine cervix.

1. The growths were divided histologically into solid and glandular forms, and a sub-division of the former into three groups according to the predominant type of cancer cell, was

found to be practicable. Of the growths 4.2 per cent were adenocarcinomata and of the remainder 30.9 per cent were spinal cell cancers, 55.8 per cent were transitional cell cancers, and 13.3 per cent were spindle cell cancers. Pure cell forms were uncommon. Only 21 per cent of the growths were pure, and in the remainder the grouping was based upon the predominant type of cell present.

2. The best immediate response to treatment was seen in the spindle cell cancers.

The radiosensitiveness of the different histological forms of cancer of the cervix is still unsettled. The results of this investigation support to some extent the biological relation between anaplasia and radiosensitivity.

3. Though the spindle cell cancers showed the better immediate results, the cellular type of the growth seemed to make but little difference so far as the results were concerned. In this respect our findings agree with those of Kimbrough and Norris.[21] This may be accounted for by a balancing of the two factors of malignancy and radiosensivity in the four histological groups.

4. Though the results in the four cellular groups are practically equal, there are small differences which are noteworthy.

(*a*) The results obtained in the group of adenocarcinomata were a little better than they were in the epidermoid cancers. Accordingly we cannot support the view that these growths are totally unsuitable for radiotherapy.

(*b*) The results in the solid carcinomata improved slightly with the degree of anaplasia of the tumour.

5. We may conclude that in this series of cases, though the cytological examination of the tumour would have supplied some information with regard to its immediate response to radiation, it would not have been of any assistance in arriving at an ultimate prognosis.

6. As special attention has been given in this study to the relation between cell type and end-result, it may be justifiably submitted that the prognostic significance of histological structure cannot be invalidated by these findings alone. However, in the course of this investigation not any feature was observed, either in the stroma or in the leucocytic infiltration, which seemed to have any bearing on the final result.

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Some Aspects of Cervical Pathology.

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THE cervix uteri, although small in size, is one of the most important structures in the female pelvis, and a large number of pathological considerations are involved in the study of its abnormalities.

In any such investigation a number of different processes have to be considered, such as the results of trauma, alterations in structure, inflammatory and neoplastic conditions, and it has to be admitted that the answer to some of the problems involved is yet to seek.

It is proposed to confine this communication to the consideration of certain local conditions of the cervix, and the first of these is a discussion of certain variations of structure which occur at various ages.

AGE CHANGES.

The influence of age on the structure of the cervix has to be appreciated in any pathological study.

Before puberty the cervix is relatively long compared with the body of the uterus and this condition persists up to the time of puberty. It represents at this stage one-half or even two-thirds of the length of the combined body and cervix as measured by the sound, compared with one-third in adult life. Normally it tapers from the vaginal attachment to the external os, and the latter aperture is round and very small. It has to be emphasized that this is the normal nulliparous condition and that it persists into adult life, so that the description of "conical cervix" and "pin-hole os" as an abnormality when found in cases of sterility and dysmenorrhoea is usually incorrect. The physical conditions present in such cases are usually not abnormal but represent merely the normal nulliparous structure of the cervix. A similar condition of os and cervix is usually found in nulliparae, in the absence of dysmenorrhoea, who later may become pregnant without difficulty,

and the contention that any narrowness of the external os can be responsible for preventing the entrance of spermatozoa cannot have any foundation in fact, since the narrowest cervix allows the passage in the opposite direction of menstrual blood corpuscles, each of which has a diameter greater than that of a spermatozoon. One is so accustomed to examining abnormalities that the normal may not be recognized.

The epthelium of the canal before puberty is columnar and in a single layer, but gland formation is relatively scanty compared with the adult. This accounts for the rarity of cervical discharges before puberty. The cells are not so closely packed as in the adult and goblet-cells are rare, but we have not been able to confirm the statement sometimes made that the nuclei are not so basal as in the adult: in our sections there has not been any evident difference in this respect. The squamous epithelium of the portio is represented by a variable number of layers, with the cells not so tightly packed as in the adult and with, here and there, a blunt papilla. The point at which these two epithelia join with each other is usually in the region of the external os, but much variation is found in this respect, especially before puberty. Most commonly such variation is shown by the columnar epithelium extending outwards to a greater or lesser extent on to the portio, forming a strawberry-red halo round the external os called a congenital erosion. But frequently the reverse is found and the epithelial junction is seen to be well inside the cervical canal, while in some cases both these appearances are seen in the same section on opposite sides of the canal. (Fig. 1.)

The transition from one type of epithelium to the other is usually gradual, but in some cases it is seen to be abrupt.

This demonstration of epithelial imbalance in the cervix, and its possible implications, is one of the most important structural features of the organ.

The adult conditions of the cervix are well known and do not require any detailed description. The adult cervix is relatively smaller compared with the body of the uterus and occupies only one-third of the organ estimated by the sound. This altered relation is, however, due mainly to increase in the size of the corpus uteri which has hypertrophied as the result of ovarian hormonal influences at puberty; the absolute length of the cervix is not materially altered.

The same tendency to irregular epithelial arrangement is present as before puberty.

After the menopause structural changes, mostly atrophic, take place. The organ becomes progressively smaller, until in time it is represented by only an elevated dimple at the vaginal vault. The time taken to bring about this atrophy has been found to vary within wide limits in different cases; while in one case it may be well marked within one year after the menopause, in another apparently similar case this regression may occupy five years.

A feature of the cervical epithelium at this stage of life is a great tendency to retain the adult appearance, even in a markedly shrunken cervix. In this way it differs from the corporeal endometrium, in which atrophic changes occur relatively early after the ovarian influence has been withdrawn at the menopause. In cervical sections up to 70 years of age, or over, well-marked and apparently normal squamous and columnar epithelium with racemose glands are seen although secretory gland-cells are few. This accounts for the fact that leucorrhoeal discharges usually clear up after the menopause. In the squamous epithelium the only change we have been able to see is a tendency to multiplication of the layers.

The fibromuscular structure of the cervix is irregularly arranged, and we have not been able to find any appearance of an arrangement into circular or longitudinal layers as reported by some other observers. It is often stated that, after the menopause, the amount of fibrous tissue is relatively increased; we have been unable to verify this statement, and sections of the nulliparous cervix at this stage of life stained by Van Gieson's stain do not show any evidence of general post-menopausal fibrosis as compared with that found in menstrual life, and apart from a pathological condition. The whole structure and not only the muscular tissue shrinks.

It is to be emphasized that our remarks so far apply only to the normal nulliparous cervix, but in studying the cervix the variability of the epithelial arrangements, and the frequency of catarrh and trauma, introduce so many variable factors that it is often difficult to be sure that a particular section is, in fact, normal. This point has always to be kept in mind in the examination of cervical sections.

The discussion of these points leads to some important considerations. It would appear that the cervix is not so much under the influence of the ovary as is the corpus uteri, and the relative smallness of the cervix compared with the body of the uterus after puberty is due, almost certainly, to hypertrophy of

the latter under ovarian influence and not to atrophy of the former. The persistence of well-marked and normal epithelium at a late age compared with the uterine body constitutes further evidence of this relative independence of the cervix of ovarian influence, and still further support is given to this view by the well-known fact that cyclical menstrual changes do not occur in the cervical mucosa.

The post-menopausal atrophy of the cervix would appear to be due mainly to reduction of blood-supply with corresponding reduction of general tissue resistance.

Trauma and Infection.

The consideration of the effects of cervical trauma brings out some important points. The main factor in producing laceration is trauma at labour, and when one remembers that, in the primipara, the external os is forcibly dilated within a few hours from a circle hardly sufficient to admit the tip of the finger to a circle with a diameter of some three and a half inches it is not a matter for wonder that a greater or less degree of laceration is usual, especially as the cervix has been previously softened by congestion and oedema in preparation for parturition. Generally the lesion is unavoidable, and while any unnecessary cervical trauma during labour such as manual dilatation, or the application of the forceps before full dilatation, is to be avoided, yet it has to be remembered that some laceration, it may be slight, usually occurs in normal labour, and that chronic inflammatory and irritative after-effects may be as marked in such a slight trauma as in a deep laceration. These after-effects, and the symptoms produced by them and their late sequelae, depend much more on the degree of infection contracted in the puerperium than on any physical extent of the laceration.

The advice so often found in textbooks and in medical papers that every cervical laceration should be sutured at labour or some 10 days later is thus seen to be impracticable in most cases and for several reasons. It may be appropriate in extensive lacerations, but these represent a small minority only; again, such suturing constitutes a difficult technical operation which should be attempted only under hospital conditions, while the majority of such deep lacerations occur in domestic practice. The usual slight laceration, however, can hardly be identified as such immediately after labour, when the cervix is normally soft and patulous with undefined limits, while the

original extent of the lesion, even if evident, might seem hardly worthy of a suture.

The almost invariable occurrence of such lesions, together with the fact that the severity of subsequent inflammatory changes and symptoms does not bear any relation to the original extent of the lesion and that such after-effects may include carcinoma, represents the most important and difficult obstetrico-gynaecological problem before us to-day.

The main immediate effects of cervical laceration are three—gaping of the wound, infection and re-infection—and on account of these features such an injury practically never heals. Lack of healing is due partly to infection and partly to the fact that the retraction of the muscular ring of the external os drags the edges of the wound apart, and in this way the parous cervix does not regain its circular contour but is represented by a horizontal line, the greater part of which represents the two surfaces which have been lacerated but have failed to heal. For this reason the statement sometimes made that cicatrization of a healed cervical laceration may interfere with dilatation and so cause obstruction in labour has seldom any foundation in fact.

It is remarkable that the cervix shows so little inclination to heal after injury while the adjacent perineum shows such an opposite tendency.

The pathology of cervical erosion has often been described, and the features of laceration, infection, ectropion, eversion, extension of columnar epithelium on to the raw area denuded of squamosa, and the reassertion of the position of the squamosa in the process of healing, have all been described and need not be recounted.

Two histological features, however, are worthy of closer examination. One of these is the probability, at least in some cases, of the epithelial appearances being due not so much to a displacement of one and replacement by another type, as to a degree of metaplasia in the existing squamous epithelium under the influence of chronic irritation. This view has been sponsored particularly by Ruge[1] and Veit,[2] but has recently been abandoned in favour of the replacement theory. It is to be remembered that all the epithelium of the genital tract comes from a common origin in the coelomic epithelium, and recent considerations by Novak[3] and others on the morphology of genital epithelium are very suggestive that epithelial metaplasia in the genital tract is more common than is usually supposed. In the case of cervical mucous polypi, which are usually

inflammatory in origin, such metaplasia is often seen, and one type of epithelium on the surface may be seen to change into the other type, while clumps of epithelial cells of indefinite structure may be found, the origin of which from squamous or glandular cells is uncertain. These changes have been studied especially by Fluhmann,[4] who gives the name of "epidermidalization" to the process.

Our investigations lead us to the conclusion that, in some cases at least, such metaplasia does occur and that the epithelial covering of the erosion represents not so much squamous epithelium displaced by columnar as a metaplasia of the squamous into columnar epithelium with its gland-forming propensities under the influence of chronic irritation (Fig. 3). Such metaplasia is shown elsewhere in the genital tract in some cases of vaginal adenomata as reported by Bonney and Glendinning,[5] and also in adenocarcinoma of the vagina as reported by the author,[6] while the occasional appearance of squamous epithelium in the body of the uterus with epithelioma there is more satisfactorily explained in this way than by the hypothetical supposition of the persistence of undifferentiated embryonic rests as suggested by Robert Meyer.[7]

The other point of importance is the manner in which infection persists in the cervix; it may do so for many years. So far as we know, the inflammatory after-effects of trauma are not so persistent in any other organ in the body.

The usual explanation is that the term "erosion" is a misnomer—that the condition is not a chronic ulcer, but that it represents an extrusion of columnar gland bearing epithelium on to the vaginal portion of the cervix. Microscopically, however, the changes of inflammation, as shown by round-celled infiltration, especially under the surface and around the glands, are well seen, and the impression is conveyed of a chronic infection constantly repeated. The explanation appears to us to lie in the fact that in a large proportion of these cases there is not any junction between the columnar and the squamous epithelium, that microscopically a raw and often small area of granulation tissue devoid of any epithelial covering usually persists between the two epithelia, and it is in cases showing these features that the signs of chronic infection continue to be seen. (Fig. 2.) Such a state of affairs may persist for years, but later, when this area becomes covered with epithelium in the process of healing, the chronic inflammatory signs clear up and are replaced by reactionary fibrosis.

A final point to be noted in connexion with cervical infection is the extent to which the condition resolves, or even disappears, after the menopause. The normal post-menopausal atrophy of the cervix has been mentioned, but such atrophic changes are most marked in a chronically infected cervix, which in menstrual life may be eroded and hypertrophied so as to form a large mass; after the menopause the organ atrophies, so that in time a small notched nodule at the vaginal vault is all that remains of this once hypertrophied cervix. The chronic inflammatory changes of erosion are practically never seen in a post-menopausal cervix, so that leucorrhoea and backache, which may have been prominent symptoms in menstrual life, usually clear up after the menopause. It has previously been mentioned that epithelial elements persist in good condition in the cervix long after the menopause, and we now see that the tendency is for the fibro-muscular tissue to atrophy markedly as the result of impaired blood-supply; this is the very opposite state of affairs to that which obtains in the body of the uterus, where the adult appearance of the epithelium is soon lost, but the muscular tissue may remain to an adult degree for long after the menopause. This represents another example of the less degree of influence which the ovarian hormones have over the cervix.

The great predisposition of the cervix to carcinoma formation is well known to be associated with the frequency of trauma and chronic infection, and the epithelial conditions mentioned are worthy of consideration in this respect. It would appear that persistence of active epithelium in this area might predispose to carcinoma late in life, especially since the general resistance of the organ is reduced by impairment of the blood-supply. In this connexion it may be noted that of 300 cervical carcinomata investigated in Cardiff Royal Infirmary, 54 per cent occurred in the post-menopausal period, while 49 per cent occurred at or over 50 years of age, when the epithelium was still active but when the blood-supply, and therefore the resisting power, was reduced.

The figures of other observers are mostly in agreement with those quoted in the foregoing, but they nearly all confine themselves to the age incidence and disregard the menopausal aspect of the matter. Thus in 347 cases compiled by Wilson[8] 223, or 64 per cent, occurred after 45 years of age; in 500 cases of Roger Williams[9] 45 per cent were in women over 45 years and 29 per cent occurred in women over 50; while in a similar number of cases investigated by Peterson[10] the percentages were 53 and

40 respectively; finally, in Weibel's[11] 800 cases, 579—about 72 per cent—occurred in women over 50 years of age.

It is suggested, as the result of the histological findings reported and the figures quoted, that one of the reasons why carcinoma of the cervix does not develop more frequently before the menopause in spite of the presence of long-continued irritation at this period is the natural resistance of the fibromuscular cervical tissue: that when this resistance is lowered after the menopause the well-formed epithelial elements are more liable to take on unrestricted growth and penetrative powers with the production of carcinoma, and that such proliferation may occur in either the squamous or columnar epithelium.

Leukoplakia and Carcinoma.

The consideration of carcinoma leads one to the further consideration of what may be the precise pre-cancerous state in the cervix. We know that 95 per cent of cervical carcinoma occurs in those parous women who are the subject of chronic infection and irritation. Cervical trauma and erosion, however, occur to a varying degree in the very great majority of parous women, while carcinoma develops in only a very small proportion of these. In hospital practice we are perhaps rather apt to overestimate the frequency of cervical carcinoma in the general female population, and we must remember that a general practitioner in an extensive practice may not see more than about one such case per year. What, then, are the factors which would indicate that carcinoma is likely to develop on one erosion and not on another? By ordinary methods of examination we have not advanced far in the direction of answering this important question. It obviously is a most important question, because if we could know that cancer, not yet present, was likely to occur in a particular case a simple amputation would save the patient from a most grave disease.

In the tongue and vulva particularly, carcinoma is preceded in a large proportion of cases by the condition of leukoplakia, while this condition almost always goes on to carcinoma formation. A similar condition in the cervix has been described by Hinselmann,[12] of Hamburg, in 1927, although it had previously been described by several authors such as De Villiers and Thérèse[13] in 1896, Verdalle[14] in 1903, von Franque[15] in 1907, and Hofbauer[16] in 1911; while more recently Ries[17] and Martzloff[18] have described cases. Hinselmann, however, has gone into the matter more systematically than his predecessors and

has come to the conclusion that it was on account of the smallness of the usual leukoplakic spots that they had for so long escaped general observation. He observed the cervix by direct binocular vision at a magnification up to 15 times with an instrument devised by him called the colposcope, and he has been able to see leukoplakic plaques of various sizes round about the external os normally invisible to the naked eye in a number of cases.

It is remarkable that a lesion so evident and widespread in the other regions mentioned should be so obscure and should require so much searching for in the cervix where its presence might be expected. In our own experience, and after keeping a sharp look-out for the condition since 1927, we have seen only one example, and that recently. Our examinations, although conducted without the colposcope, have been searching and have involved the naked-eye and microscopic examination of several hundred cervices.

The leukoplakic patches have always been seen on the vaginal surface of the cervix and may be, as stated, invisible to the naked eye or up to one centimetre in diameter; they are pale, sharply defined, and slightly elevated. In our case there were two areas, one on the anterior and one on the posterior lip of the cervix, each just under one centimetre in diameter.

On microscopic examination two chief characteristics are seen: (1) the changes are proliferative without being penetrative, and (2) the changes are sharply limited to a particular area of squamous epithelium, so that the change from normal to pathological is sudden. (Fig. 4.)

In the first place the cells are closely packed and of irregular shape; they do not show the regular differentiation into basal, Malpighian, and flattened surface layers, while the amount of surface cornification is not great. The protoplasmic bridges between the Malpighian cells are not well marked and may be absent, while the finger-like processes penetrate to varying depths into the stroma and, if the section be cut obliquely, the deep part of the epithelial column separated from the surface cells looks very like epithelioma.

The squamous epithelial layer is thicker than usual and the cells and nuclei take the stain more deeply than normal squamous cells, in this way resembling epithelioma cells. The important point to regard is the appearance of the deepest cells which typically do not break the bounds of the basement membrane, and in this way alone are unlike carcinoma cells. The papillae tend to be numerous and narrow. At the margin of

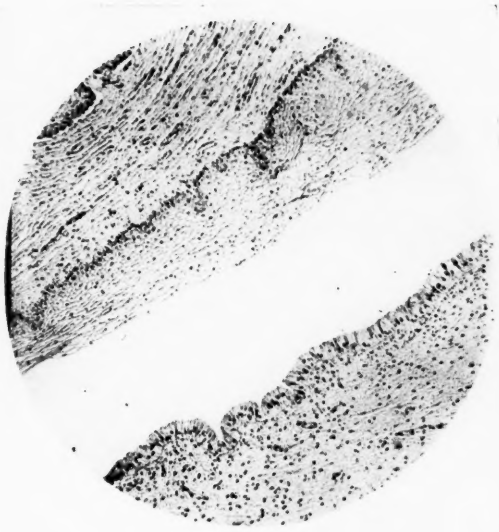

FIG. 1. Low power photomicrograph of the cervical canal of an infant. It is seen to be lined on the one side by squamous and on the other side by columnar epithelium.

FIG. 2. Photomicrograph, low power, of the surface of a cervical erosion showing the edge of the squamous epithelium with the adjacent raw area bare of epithelium and infiltrated by small cells.

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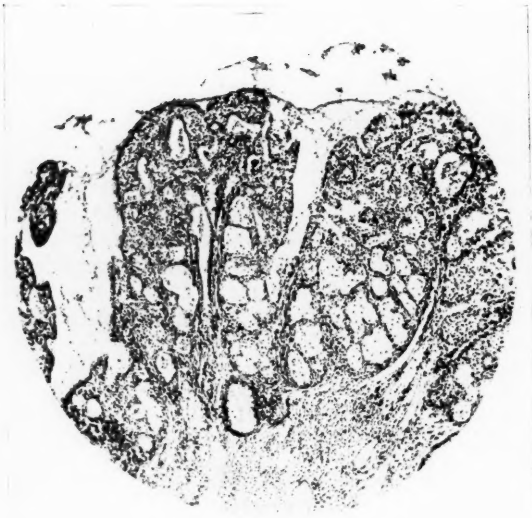

FIG. 3. This shows the surface epithelium on an erosion. The histological structure of the cells is so indefinite that their origin from squamous or columnar epithelium can hardly be determined.

FIG. 4. Low power photomicrograph to show the edge of a patch of leukoplakia of the cervix. The abrupt transition to normal at the edge of the patch is seen as well as the irregular structure and arrangement of the constituent cells.

the condition a sudden and striking change in appearance to the normal is seen, and this is one of the most characteristic features.

Until a few years ago many observers doubted the existence of such a condition as leukoplakia, and we were sceptical before the present specimen presented itself. Hinselmann, however, has been able to collect 110 cases up to 1929, while in six other cases reported in the literature carcinoma was seen to develop on leukoplakic patches.

It would appear, then, that leukoplakia is the connecting link between erosion on the one hand and carcinoma formation on the other, and it is remarkable that it has been so long in being discovered. Obviously the matter requires much further investigation and we have to be very careful lest any and every white spot on a cervix is described wrongly as leukoplakia.

From the account of the histology given above it will be seen that the appearances may often resemble actual carcinoma and that, in a particular section, views may be divided on the subject.

One important application of these considerations is that it helps further to elucidate the actual site of origin in the most common type of carcinoma met with, the epithelioma or epidermoid carcinoma, in the cervix. It is usually stated, and in our opinion rightly, that the majority of cervical carcinomata are epitheliomata taking origin from the squamous epithelium of the portio. But from time to time this is disputed and the appearances seen are regarded as extreme metaplasia of columnar or glandular carcinoma from the cervical canal. We have all seen many sections in which, with well-marked metaplasia and degeneration present, it has been difficult or impossible to state the parent tissue, but the histological characters of the majority of such sections leaves little doubt about their squamous origin. This matter was discussed recently in correspondence in the *Lancet*[19] and the opposing views are well put there.

But the isolation of leukoplakia as an immediate pre-cancerous condition and its invariable occurrence in connexion with squamous epithelium not only in the cervix but elsewhere, as in the tongue and vulva, appears practically to settle the matter in favour of a squamous origin in the majority of cases.

Carcinoma and Procidentia.

Consideration of the factors predisposing to carcinoma formation in the cervix would be incomplete without regarding its relation to procidentia. It is generally agreed that the chronic

irritation of erosion is a most important predisposing factor to carcinoma. But in procidentia not only is this factor present as usual but it is further supplemented and aggravated by long-continued irritation by clothing with the production of true ulceration. Conditions more ideal for carcinoma production could hardly be imagined, yet the association of these two conditions is most rare and the majority of observers have never seen a case. In this respect we have had the unusual experience of two cases of this association and one of these was accompanied by a large rectal prolapse. The details of these cases will be presented in a later communication.

Cases have also been reported by Russell Andrews,[20] Barbour Simpson,[21] Petersen (two cases),[22] Chalfant,[23] Schmitz[24] and others, but they are rare.

The cause of this unexpected infrequency of association between these two conditions is puzzling and obscure. In 1931 Delvaux,[25] who had himself never seen a case, sought the opinion of several continental gynaecologists on the matter, and received from each one who replied a different explanation. Faure,[26] of Paris, made the surprising statement that the association was not rare as procidentia itself was uncommon! Hamant was of opinion that exposure to the air and free drainage of discharges were important factors; Leriche ascribed the immunity to chronic congestion and stasis; Menge thought that the evaporation and hence dissipation of acid vaginal discharges was important; Forgue was of opinion that procidentia usually occurred in those over the cancer age; while Grégoire and Savariaud believed that infections of the prolapsed cervix were uncommon and hence carcinoma was not predisposed to. Delvaux, after considering these diverse views, ascribed the rarity of carcinoma in prolapse to a special cancer immunity. This, however, is merely begging the question and does not offer any attempt at a rational explanation.

The factors concerned in this phenomenon appear to be mainly two.

Congestion of the cervix is nearly always present in procidentia and it is a generally accepted pathological opinion that carcinoma is less likely to occur in a congested tissue. This supports the view previously expressed that the reduction of the cervical blood-supply at the menopause makes the organ more vulnerable to epithelial proliferation. Non-retention of irritating discharges is the other factor concerned, and its importance is probably great. It demonstrates how potent accumulated

vaginal and cervical discharges must be in this respect if their absence can neutralize the effect of long-continued physical irritation and ulceration as occurs in procidentia. Age incidence can have little to do with it, as the large proportion of cervical carcinomata appearing after the menopause has previously been stressed.

Our conclusions and observations, both clinical and pathological, have been given from a personal point of view with due regard to the opinions of others. But the main purpose of the communication has been to demonstrate the complexity of so many of the problems of cervical pathology and the necessity of still further research in their elucidation.

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A Study of Ureteral Tone During Pregnancy.*

BY

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SINCE the problem of the activity of the uterus, which has been the main subject for discussion at this meeting, is probably closely associated with that of the ureters during pregnancy, I venture to bring before you this preliminary communication regarding a method of estimating ureteral tone.

It is now well known that dilatation and stasis occur in the ureters very frequently during pregnancy, believed by some to be due to an atony which is a normal accompaniment of pregnancy, by others to be due to pressure on the ureters by the pregnant uterus. It is likely that both factors play a part in the production of the dilatation and stasis but it is difficult to estimate their relative importance.

There is no doubt that the uterus does compress the ureters at the level of the pelvic brim, but this does not constitute the sole factor in the production of the dilatation for several reasons. First, the amount of dilatation and kinking is very much greater than that produced by tumours of similar size in non-pregnant women; secondly, the dilatation reaches its maximum about the sixth month of pregnancy, and in many cases diminishes towards term, despite the increase in size of the uterus; and thirdly, it varies in different patients much more than one would expect. Some other factor must exist.

From the evidence supplied by chromocystoscopy and intravenous pyelography it seems likely that atony of the urinary tract occurs early in pregnancy, and increases as the pregnancy advances, so that at the fourth month even the soft uterus pressing on the ureters at the pelvic brim is enough to cause dilatation and stasis above this point. Towards term the atony disappears so that although the pressure of the uterus is now greater, the stasis

* This work is being carried out with the aid of a grant from the Medical Research Council.

is less and, in some cases, pyelograms show that the dilatation also is less. In the puerperium atony, of the urinary tract again occurs, but this is difficult to detect by chromocystoscopy and intravenous pyelography, as there is now no stasis from the pelvic brim upwards, the pressure at the pelvic brim now being relieved owing to the involution of the uterus.

Dilatation and stasis are more marked in primigravidae as will be seen from the following figures, taken from a series of 51 healthy pregnant women, 29 primigravidae and 22 multiparae, who were examined repeatedly during pregnancy by chromocystoscopy and intravenous pyelography.

	Little or no stasis	Moderate stasis	Marked stasis
Primigravidae ...	8 or 27.6 per cent	14	7 or 24.1 per cent
Multiparae	14 or 63.6 ,, ,,	8	0

Possibly the superior tone of the abdominal muscles is the factor responsible for the increased incidence in primigravidae, since in these cases the uterus is bound to exert greater pressure on the pelvic brim than when the abdominal wall is lax, so that the uterus can fall forward. By the methods already mentioned a direct estimation of the ureteral tone is impossible, so that we are unable to ascertain whether the variations in the amount of ureteral stasis and dilatation present in different cases are due to variations in tone, or to variations in pressure on the pelvic brim. The method I have adopted to estimate the tone of the ureteral musculature directly is as follows.

A catheter is introduced into the ureter, of such a diameter as to fit exactly. It is connected by means of rubber tubing to a water manometer and the height to which the ureter can force a column of water is measured. The catheter is then connected to a reservoir into which the urine drains. This reservoir is of such a size that fairly large quantities of urine collected from the ureter will make very little difference to the height of the fluid in it. The ureter, therefore, for practical purposes is acting against a constant pressure. From the top of the reservoir a tube is led off and connected to a float, recording lever and drum. The urine displaces air which causes the lever on the drum to rise. The rapidity with which the lever rises gives a record of the rate of excretion of urine and, although it is only a volume recorder, peristaltic waves are sometimes seen. At

intervals the lever has to be brought down to the base line, as it tends to rise continuously. The reservoir can be set at any convenient height and the rate of outflow of urine compared at various heights. The rate of excretion of known quantities of fluid injected into the ureter can also be used as a measure of ureteral tone. On all occasions the tracings were taken from the right ureter. Each unit on the horizontal line represents one minute, and on the vertical line two cubic centimetres. "L.P." on the tracing means that the ureter is working against low pressure, that is, with the reservoir at a height of two to five centimetres above the level of the kidney, "H.P." high pressure, an increase in height of the reservoir by 10 centimetres. In other cases the actual pressure against which the ureter is working is marked in centimeres of water. "S" indicates that the patient sat up or in some way increased the intra-abdominal pressure. "Below brim" indicates the point at which the ureteral catheter was withdrawn below the level of the pelvic brim. "H. and K." means that the patient was placed in the knee-elbow position.

The tone of the ureter has been found to vary in different parts of it, as has been pointed out by Kreutzmann[1] and Trattner[2] in the non-gravid state. There are technical difficulties in the way of estimating this in the later months of pregnancy, but in the early months it can often be observed, e.g. a healthy primigravida two and a half months pregnant supported a column of 16 centimetres in the upper part of the ureter and 22 centimetres in the lower.

The type of tracing obtained varies according to whether the patient is in the early or later months of pregnancy. This is shown in Fig. 1.

"A" refers to a healthy primigravida, two months pregnant, and "B" to a woman who had just recovered from an acute attack of pyelitis seven months pregnant with her second child. In A peristaltic waves can be seen, and although the reservoir was raised and lowered by as much as 10 centimetres a difference in the rate of excretion is not observed. In the upper part of the tracing we see that the rate of excretion is greatly increased after giving five cubic centimetres of dilute acriflavine, which caused pain, and the peristaltic waves are less marked, suggesting more continuous activity of the ureter. The catheter was pulled below the pelvic brim at the point indicated, but a difference in the tracing did not result except that the waves became bigger. We conclude from these observations that the ureteral tone is good and that there is not any delay at the pelvic brim.

In the case of B, the ureter above the pelvic brim supported 15 centimetres of water but, by increasing the intra-abdominal pressure, by asking the patient to sit up or strain, the column supported could be raised to 30 centimetres or more; so soon as the intra-abdominal pressure was lowered it fell again to 15 centimetres. The lower tracing shows the rate of excretion at very low pressure (two to three centimetres). If the height of the reservoir is raised then the rate of the excretion falls off but immediately the abdominal muscles are tightened the rate of excretion increases. In the upper tracing at the point indicated, when the catheter is pulled below the pelvic brim a cessation of excretion immediately follows, as indicated by the horizontal line. As is seen from the pyelogram in Fig. 2, the lower portion of the ureter is also dilated and atonic so that an increase in the intra-abdominal pressure by sitting up is followed by a rise in the lever. When the abdominal pressure is increased in the same way, however, a rise in the lever is not recorded since the lower portion of the ureter has been emptied and urine has not yet come from above the pelvic brim. As is seen in the tracing, massage over the kidney causes some urine to flow over but this occurs in much larger amounts when the patient is turned on her hands and knees. This experiment was repeated a second time with the same result. On asking the patient to sit up, a more rapid rise results, but on repeating this a rise of the lever does not occur, as the lower part of the ureter is now empty again. In this case, therefore, the right ureter is compressed at the pelvic brim, and so long as the catheter is above the pelvic brim increase of intra-abdominal pressure, by tightening the recti muscles, increases the rate of excretion, whereas, with the catheter below the pelvic brim, increased intra-abdominal pressure increases the compression of the ureter at the pelvic brim and urine does not escape. The tone of the abdominal muscles, therefore, appears to be important in determining the amount of compression of the ureters at the pelvic brim. This patient B went to term after making a good recovery from the acute attack by treatment with simple remedies.

This case is in contrast to another, a multipara in whom the pregnancy had to be terminated. She had been treated by indwelling catheters, and while they were in position she felt well and the temperature remained normal. When the catheters were taken out the temperature rose again and the general condition became worse. The ureters in this case could only support a column of water of four centimetres. After the termination of

the pregnancy the condition cleared up very quickly. It seems reasonable to assume that the prolongation of the pyrexia was due to the fact that the ureters were too atonic to overcome the pressure exerted by the uterus, so that a marked degree of stasis persisted.

As has been mentioned already, stasis occurs in the right ureter from the fourth month onwards. Fig. 3 is a pyelogram of a healthy primigravida, four months pregnant, in whom the urine is sterile.

Dilatation of the right urinary tract, calyces, renal pelvis and ureter to the pelvic brim is clearly shown. The tracing in this case (Fig. 4) supports the view, which many are inclined to doubt, that the uterus can compress the ureter at this early stage of pregnancy. The reservoir was first set at the low pressure of two or three centimetres; and 30 cubic centimetres of acriflavine were injected without causing any pain; a rise in the lever resulted. The effect of increasing the height of the reservoir by 10 centimetres is shown to diminish the rate of excretion but not to stop it. Twenty cubic centimetres were again injected to make sure that the upper part of the ureter was full and the catheter withdrawn below the pelvic brim at the point indicated. A complete cessation of flow followed. When the patient again sat up a flow of urine followed and the adoption of the hands and knees position gave a similar result, but a return to the dorsal decubitus caused the flow to stop immediately. These changes of posture were repeated with the same results. The probable explanation is that the knee-elbow position caused the uterus to fall forward, away from the pelvic brim, and so to relieve the compression of the ureter. Later in the pregnancy the same experiment was repeated and did not give such striking results, probably because the increased size of the uterus leaves less room for it to fall forward. In some cases the compression of the ureter is relieved in the same way by placing the patient on the left side. This does not occur with the patient lying on the right side.

If the amount of delay in excretion were dependent entirely on the tone of the ureter, then one would expect to find the same amount of dilatation and delay in ureters with equal tone. In both the following patients the ureter in its upper half supported a column of water 20 centimetres high. In the first patient (see Fig. 5, lower tracing), there was not any delay in excretion, the delay in the excretion of indigo-carmine being four minutes at both orifices. In the second patient (see Fig. 5, upper tracing), there

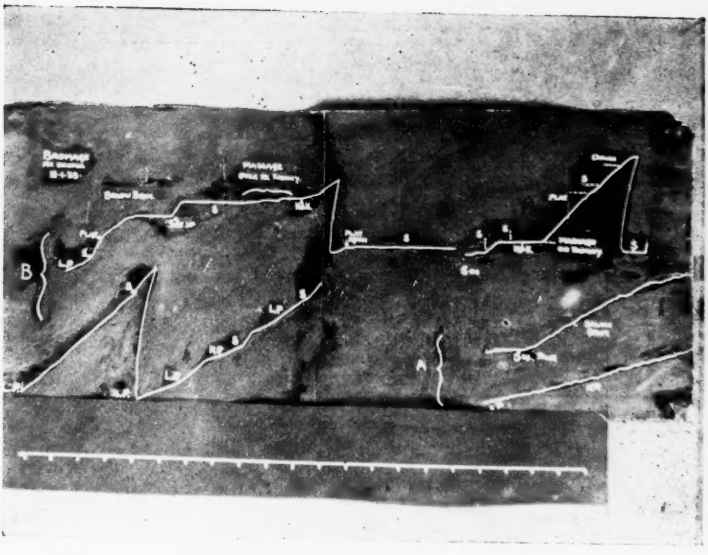

FIG. 1.

FIG. 2.

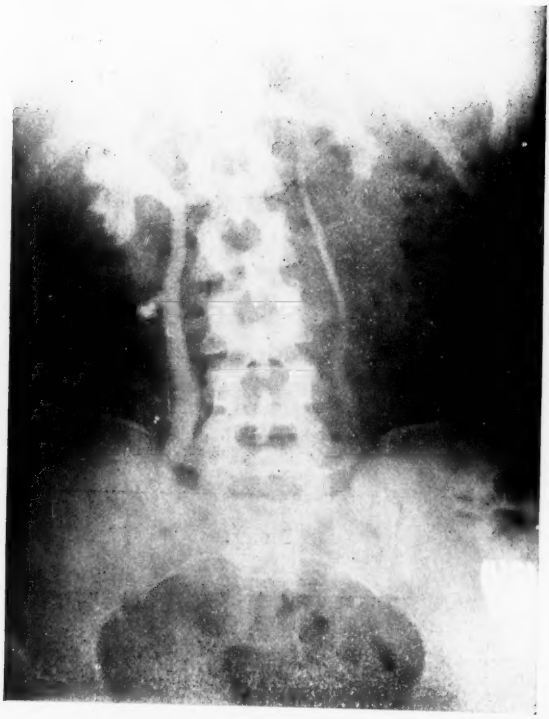

FIG. 3.

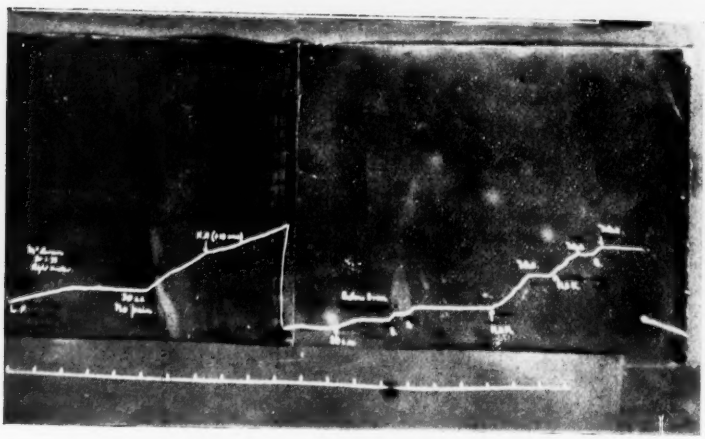

FIG. 4.

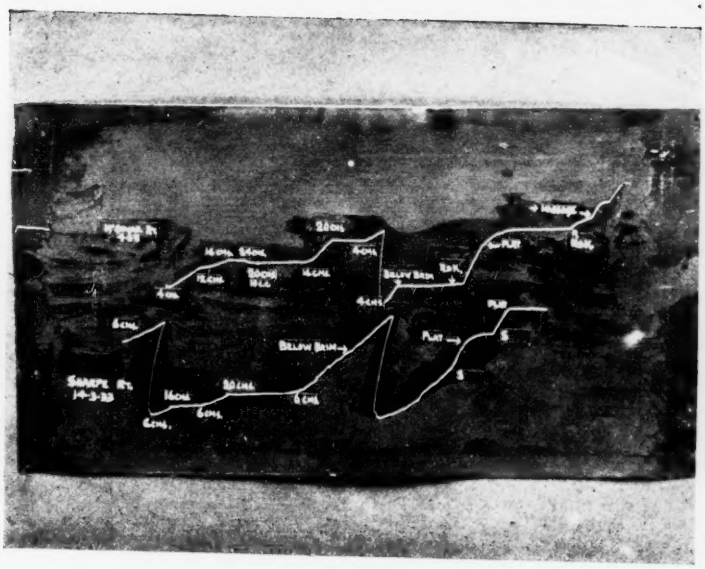

FIG. 5.

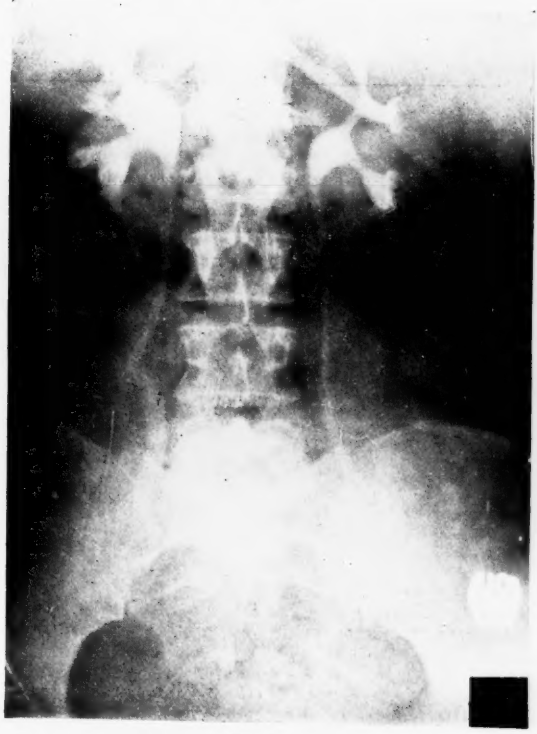

FIG. 6.

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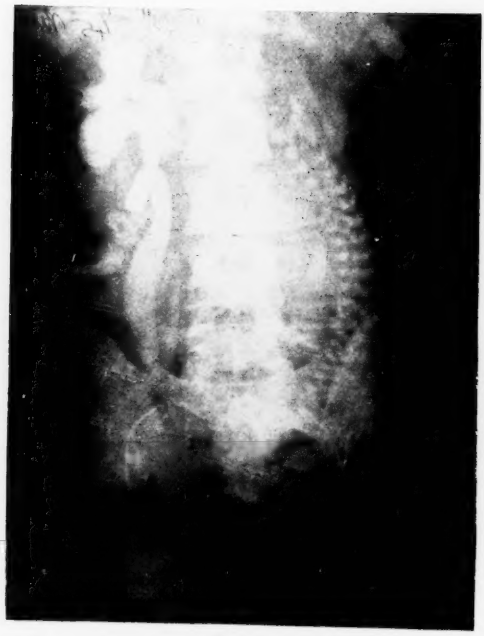

FIG. 7.

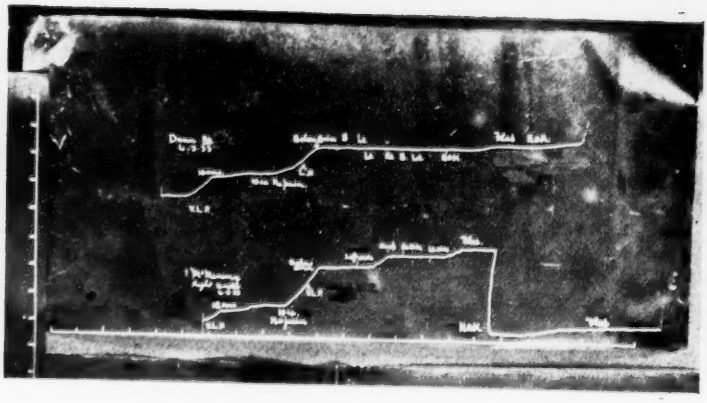

FIG. 8.

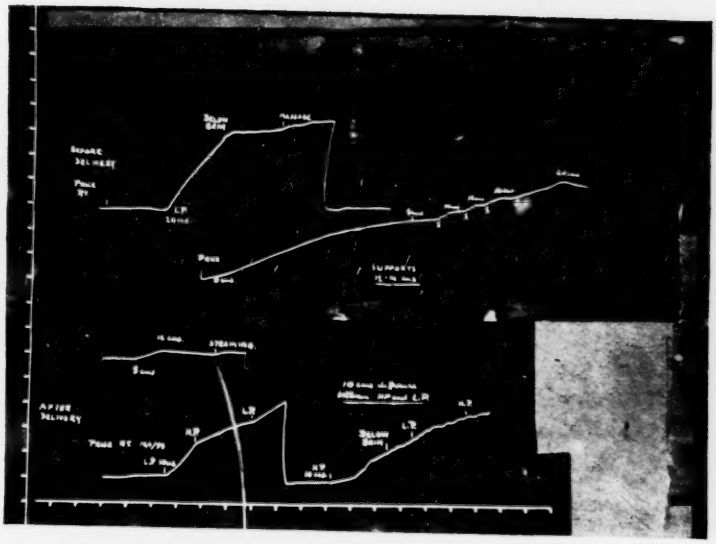

FIG. 9.

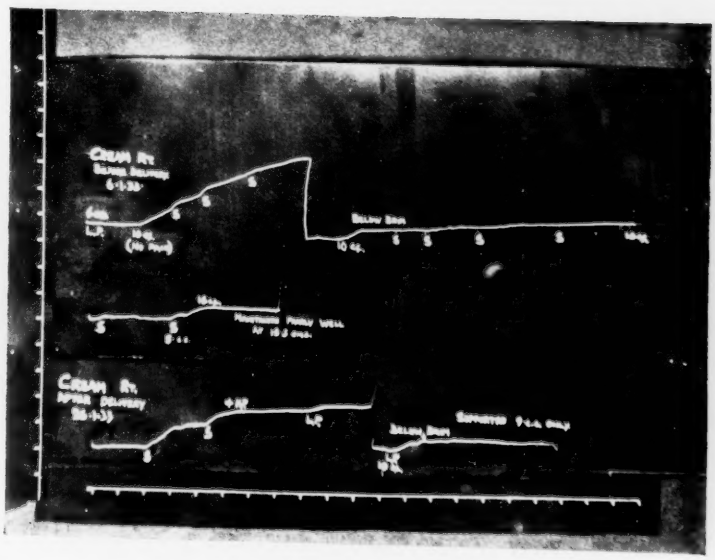

FIG. 10.

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was marked delay at the right side, the dye not having appeared in 15 minutes.

As will be seen from these tracings, the urinary flow through the catheters practically stops when the pressure is raised to 20 centimetres.

In the second patient (upper tracing) at a pressure of 24 centimetres the urine is seen to flow back into the ureter. In both instances the excretion is rapid at low pressure. In the first patient (lower tracing) when the catheter is pulled below the pelvic brim, the excretion continues, whereas in the second it stops, to be re-established when the patient assumes the knee-elbow position. It seems likely that the pressure exerted on the ureter at the pelvic brim is greater in the second case than in the first. The indigo-carmine findings and the tracings suggest that in the first patient there is very little dilatation of the urinary tract. This is confirmed by the intravenous pyelogram (see Fig. 6), which shows very slight dilatation and kinking of the right ureter, with very little displacement outwards.

Figure 7 is a pyelogram of a healthy primigravida, seven months pregnant, which, in sharp contrast to the case just described, shows marked dilatation and kinking of the right urinary tract above the pelvic brim, although the tone in this part of the tract is so good as to support a column of 30 centimetres.

The tracing from this patient (Fig. 8, lower tracing) shows that even with the pressure at 12 centimetres, 10 centimeters of acriflavine injected causes a sharp response, but as soon as the catheter is pulled below the pelvic brim the secretion stops.

Within a short time of placing the patient in the left lateral position, the secretion starts again, to stop immediately she is placed on her back. Turning her on to the right side has no such effect. In this patient, therefore, in spite of the ureter having good tone, there is a marked dilatation and stasis above the pelvic brim. The abdominal muscles were well developed and tense, and this may afford the explanation.

It is evident, therefore, that there are two important factors in the production of stasis, the tone of the ureter and the pressure of the uterus on it at the pelvic brim. The pressure of the uterus is necessarily an ever increasing one, so that the decrease in the stasis which takes place near term despite this must depend on improvement of the ureteral tone.

Chromocystoscopy and pyelography show definitely that the stasis is less near term than at the sixth or seventh month; for

example, the following are the indigo-carmine excretion findings at monthly intervals during pregnancy in a healthy primigravida.

	Left side	Right side	
4 months	4 mins.	4 mins.	
5 ,,	5 ,,	5 ,,	
6 ,,	10 ,,	17 ,,	(no dye)
7 ,,	6 ,,	10 ,,	
8 ,,	4 ,,	5 ,,	

Just before delivery, by chromocystoscopy, the ureters appear to be acting vigorously, the efflux being regular and strongly expelled. In the puerperium, on the other hand, the efflux is often lacking in power and irregular in its time of appearance and size, suggesting atony. As the uterus is now a pelvic organ it no longer presses on the ureters at the pelvic brim, so that the indigo-carmine excretion time is now less and may even be normal, despite the atonic condition of the ureters. The following case illustrates these points (see tracing, Fig. 9).

Before delivery, the indigocarmine time was four minutes at the left side and five minutes at the right. At 14 days after delivery, the indigo-carmine time was seven minutes at the left and nine minutes at the right side. The contractions at the right side were irregular. Before delivery, the right urinary tract supported a column of 12 centimetres, and after delivery, slightly less. Before delivery (see Fig. 9, upper tracing), when the catheter is withdrawn below the pelvic brim, at the point indicated, excretion stops abruptly, whereas after delivery (Fig. 9, lower tracing), withdrawal of the catheter below this point has no effect on the outflow, and bigger peristaltic waves than with the catheter in the upper part of the ureter are seen, since the whole ureter is now taking part in their production.

Further, in seven out of eight healthy women examined before, and again at eight or nine days after, delivery, a distinct lowering of tone was noted in the puerperium; e.g. Fig. 10 is a tracing from a healthy primigravida, in whom before delivery the ureters supported a column of 16 centimetres and after delivery only nine centimetres.

The lower tracing in Fig. 10, taken after delivery, shows that the ureter is still very susceptible to pressure from without. A rapid increase in the rate of excretion occurs when the intra-

abdominal pressure is raised by the patient sitting up and, when the reservoir is raised, the excretion quickly stops. The response to the instillation of 10 cubic centimetres of acriflavine is less rapid than during pregnancy and, on pulling the catheter below the pelvic brim, the excretion stops, as it does during pregnancy.

In several patients, also, the injection of 10 cubic centimetres of acriflavine, which caused pain before delivery, did not cause any after delivery.

The most striking example of this loss of tone after delivery occurred in a patient suffering from albuminuric toxaemia, in whom the upper part of the ureter before delivery supported a column of water of 36 centimetres, while after delivery it supported only six centimetres. A catheter which exactly fitted the ureter before delivery was found to be much too small after delivery, so that to prevent leakage a larger catheter was required. This in itself indicates atony. It has been my experience that patients suffering from albuminuric toxaemia have very little delay in excretion, as determined by chromocystoscopy, and in a few cases, in which the tone has been tested by the method under consideration, it has been found to be very good.

It has been shown by Robson[3] and others, that the activity of the uterus, as judged by its response to pituitrin, varies at different stages of pregnancy. It is practically insensitive to pituitrin until the sixth month of pregnancy, from which time until term it becomes increasingly more sensitive to small doses. Within a few days of delivery it is again insensitive to it. These variations correspond, in time, to the variations in the activity of the ureter as determined by the various methods described, since we have shown that the ureters are most inactive about the end of the sixth month, and that their activity improves steadily towards term. In the puerperium they again become less active. In patients suffering from albuminuric toxaemia there is excess of posterior pituitary hormone in the circulation (Anselmino, Hoffmann and Kennedy,[4] 1932), and in these cases we know that there is very little atony of the ureters. These findings suggest that the posterior pituitary hormone may be responsible for the increased tone of the ureters as pregnancy advances.

The conclusions reached fall into line with clinical experience. Pyelitis of pregnancy follows the production of stasis and, therefore, most commonly occurs between the fourth and sixth

months. It affects primigravidae more severely than multiparae in whom the lax abdominal wall, as we have seen above, prevents undue compression of the ureters by the uterus. Patients with marked stasis, with or without urinary infection, have a normal or low blood-pressure and do not develop albuminuria of pregnancy. On the other hand, women who develop albuminuria and a rise of blood-pressure during pregnancy seldom develop pyelitis and in the very few cases in which urinary infection has been observed it has been transitory. It is interesting to note that these patients are specially susceptible to pyelitis of the puerperium, probably because the hormonal influence which prevented stasis in pregnancy has now been withdrawn.

The work is only in its initial stages and the apparatus is somewhat difficult to perfect. Many points remain to be investigated, such as whether the ureter varies in its response to pituitrin at different stages of pregnancy, in the same way as the uterus. I feel sure that investigations along those lines ought to throw further light on the factors influencing the activity of the ureteral musculature during pregnancy, and so lead to the adoption of measures to prevent stasis with its sequelae.

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The Innervation of the Uterus.

BY

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NOT only on account of its fundamental relation to the problem, but also because of its very controversial nature, no preliminary to the study of the mechanism of uterine action is of more importance than that entailing a consideration of the nerve supply to that organ.

In the following pages an attempt will be made, by correlating the writer's cadaveric and operative researches in this subject with those already published, to provide a reasonably standard description of the innervation of the uterus in its various aspects. The personal researches referred to include dissection in 60 cadavers, stillborn children and foetûs, and the examination of 30 specimens removed by operation.

(*a*) *The Extrinsic Supply.* (Fig. 1).

For descriptive purposes the extrinsic nervous system of the uterus may be divided primarily into its central and peripheral constituents, and the latter conveniently subdivided into its three anatomical components, i.e. the abdominal and pelvic roots and the junction of these two in the pelvic plexus. On account of the exceedingly hypothetical nature of the central connexions of the uterine nerves, consideration of these will be postponed until a later chapter, and attention directed primarily to the peripheral section, in the order classified above.

The abdominal autonomic system supplies the pelvic plexus, via the solar plexus, the intermesenteric nerves, and the superior, middle and inferior hypogastric plexuses, in that order from above downwards. In addition, contributory branches arise from the ganglia of the lateral sympathetic chain in the abdomen and pelvis. The solar plexus must be taken as the most cranially placed structure in this long tract, as it is imposisble to trace individual fibres through its ramifications; for the same reason an approximately similar level may be taken in the ganglionated sympathetic cord.

The solar plexus stretches across the front of the abdominal aorta at its commencement, at the level of the first lumbar vertebra. It covers the anterior surface of the vessel from the coeliac axis to the origin of the renal arteries, and extends for some distance laterally on each side of it, lying upon the crura of the diaphragm. The solar plexus consists essentially in a number of ganglia of varying size joined by a feltwork of interlacing communications, and though the consequent difficulty of accurate dissection, and the extreme variations met with in different specimens make description difficult, the configuration portrayed in Fig. 1 may be accepted as a reasonable attempt, representing, as it does, the average disposition in a series of 10 dissections.

The contained ganglia are arranged in pairs, the semilunar, aortico-renal and renal ganglia of each side, in that order from above downwards. They receive from above the greater, lesser, and least splanchnic nerves, and distribute peri-arterial plexuses to the neighbouring vessels and primary roots to the intermesenteric nerves.

The intermesenteric nerves, intermesenteric plexus (Hovelacque), superior aortic plexus (Beck), lumbo-aortic plexus (Hirshfeld, Cruveilhier), abdominal-aortic plexus (Schwalbe Deaver, Ranson), correspond to that portion of the "pre-aortic plexus" which is situated between the two mesenteric arteries. The intermesenteric nerves consist of from one to three separate parallel nerves of fair thickness and tough consistence, lying along the anterior-lateral borders of the aorta. (A true pre-aortic plexus, *per se*, is non-existent, in spite of the authority of Haller,[1] Tiedmann,[2] Valentin,[3] Sappey,[4] Beck,[5] Hirschfeld,[6] Frankenhauser,[7] Schwalbe,[8] Dahl,[9] Deaver,[10] and Ranson[11] to the contrary.) A true pre-aortic plexus was originally suggested by Lee,[12] and Henle,[13] in the middle of the last century, but it is only within recent years that anatomists have begun to appreciate the fallacy, the result of false dissection in the aortic adventitia.

Laterally the intermesenteric nerves receive fine branches from the ganglia of the lumbar sympathetic chain, and occasionally from the inter-ganglionic part of the chain itself. These branches, though easily identified, are of extremely fine consistence, and I cannot subscribe to the finding of Laux,[14] and Learmonth,[15] to the effect that they, and not the solar plexus constituents of the intermesenteric nerves, are of primary importance in the pelvic sympathetic supply.

The superior hypogastric plexus, or presacral nerve, represents the continuation downwards of the intermesenteric nerves below the level of origin of the inferior mesenteric artery. At this level the nerves deviate medially from their position upon the antero-lateral aspect of the aorta to gain its anterior surface, converging, after receiving a branch from the inferior mesenteric ganglion, to form the so-called "presacral nerve." I have previously[16, 17] described in detail the anatomy and surgery of this important, but unfortunately-named, structure (it is prelumbar rather than presacral, and rarely takes the form of a single nerve), and a short summary only of its more essential characteristics need be given here.

The nerve or plexus lies anterior to the bodies of the fourth and fifth lumbar vertebrae and their intervening disc, separated from the bone by the left common iliac vein in its upper part, and below by connective tissue and the middle sacral artery only. It runs vertically downwards, a little to the left of the mid-line, and occupying, according to its different formations, a varying amount of the interiliac space. The whole plexus is ensheathed by a condensation of the subperitoneal areolar tissue, to which it is closely adherent; but as the sheath itself is only loosely attached to the surrounding tissues, the plexus-containing envelope may be easily removed without damage to the neighbouring structures, a fact of considerable surgical importance.

The form exhibited by the superior hypogastric plexus varies widely. Most commonly a somewhat narrow plexus of two or three parallel intercommunicating nerves is present, but this may be replaced by a wider plexus similarly constituted, or by a single narrow true presacral nerve. This last, however, although stated by Latarjet to be the most common configuration, is comparatively rare (10 per cent of cases).

The presacral nerve merges below into the middle hypogastric plexus (Fig. 1), a flat triangular fenestrated sheet of neurofibrous tissue lying upon the posterior pelvic wall, at or just below, the level of the promontory. The middle hypogastric plexus contains many interlacing fibres, and is closely adherent posteriorly to the fascia covering the middle sacral artery, rupture of which vessel is a common accompaniment of attempts to elevate the plexus.

The inferior hypogastric plexuses, lateral hypogastric plexuses (Cordier, Morrison-Lacombe), hypogastric nerves (Latarjet), arise from the extremities of the lower border of the middle

hypogastric plexus, or, in the absence of the latter, as the direct continuation of the bifurcated presacral nerve, or plexus. Each inferior hypogastric plexus consists of two or three parallel nerves interlacing in a complicated manner to form a long narrow plexus, which runs downwards, outwards and at first backwards to gain the posterior extremity of the corresponding uterosacral (sacro-vaginal) fold. Upon entering the fold the constituent nerves of the plexus come into intimate association with the sacral fibres of the utero-recto-sacral ligament, and run downwards, outwards and forwards upon the lateral aspect of the ampulla of the rectum, to gain the postero-superior angle of the pelvic plexus, in which they terminate, furnishing the sympathetic root proper to that structure. In its course each plexus passes behind the common iliac vessels, being separated postero-laterally from the levator ani and the sacral plexus by the parietal pelvic fascia.

The pelvic roots consist of the nervi erigentes, and fine twigs from the ganglia of the sacral sympathetic chain.

The nervi erigentes are long fine nerves of considerable strength, varying in number from two to four, the constituents communicating in a plexiform manner. The nervi erigentes arise from the medial aspect of the anterior primary divisions of the intermediate sacral nerves, one to two centimetres from their foraminal exit, and pass forwards and slightly outwards within the utero-sacral folds, lying somewhat above the level at which the peritoneum forming those folds is reflected on to the pelvic wall and pouch of Douglas. With the exception of some filaments to the upper vagina and rectum the nerves are distributed entirely to the pelvic plexus, forming the medial sheet of the bilaminar plexus.

The particular sacral trunks which give origin to the nervi erigentes have been the source of some dispute. Kehrer[19] specified the second and third; Luschka[20] the third and fourth; Rein[21] the third alone; Frankenhauser[7] and Waldeyer[22] the second, third and fourth; Henle[13] "the third and fourth, and sometimes the second." Cordier,[23] who has recently investigated this problem, states that "constantly each sacral nerve sends one or several branches of size to the hypogastric ganglion." Cordier found the first sacral nerve to supply two branches two centimetres from its exit; the second and third three branches each, at one centimetre from their exit; and the fourth two branches, at three milimetres from its foraminal emergence. In a series of 10 consecutive dissections I found the incidence to be as

follows: In six cases the second and third anterior sacral divisions contributed the nerves, in three the third and fourth, while in only one case did the second, third and fourth combine for this purpose. Perhaps through faulty dissection, I have been unable to verify in my specimens the supply from the first sacral nerve upon which Cordier is so insistent.

The roots from the sacral sympathetic chain are two or three fine twigs which arise from the middle ganglia of that structure, to pass to the posterior border of the pelvic plexus. Cordier states that only the last sacral ganglion furnishes branches directly to the pelvic plexus, the other supplying that structure by means of numerous communications with the sacral nerves. I have been unable to verify this in more than two of my own specimens; in the rest the direct pathway described above was followed in each case.

The pelvic plexus, hypogastric ganglion (Latarjet), lateral cervical plexus, utero-vaginal plexus, ganglion cervicale uteri of Lee, plexus of Frankenhauser, is a quadrilateral bilaminar sheet of neuro-fibrous tissue lying on each side upon the lateral aspect of the rectum. It varies somewhat in size, measuring approximately three centimetres antero-posteriorly; two centimetres vertically; and one millimetre in thickness; but the size of the plexus is not relative to the age of the subject, attaining as it does in the new-born child to about half its adult dimensions. In all cases, however, its very considerable size "astonishes the dissector who sees it for the first time" (Latarjet and Bonnet). When first encountered the plexus appears as a flat uniform sheet, but this is fairly easily fenestrated by removal of its fibro-fatty supporting tissue, a procedure which, however, does not alter the general outline of the plexus. Close dissection of the structure reveals it to be composed essentially of several parallel nerve bundles of considerable size and strength, the continuation of the inferior hypogastric plexus and nerve erigentes, bound together by many equally strong nerve communications and bands of fibrous tissue, but still retaining a roughly quadrilateral form. This description differs from that given in some of the more recent French writings, but it appears to me that configuration of a bundle of many very fine nerve-fibres illustrated and described by Hovelacque[24] and Segond[25] under this heading is the result of dissection much closer than that required by ordinary anatomical standards.

The plane of the plexus is inclined with the lateral pelvic wall at this level, so that one of its surfaces is postero-infero-lateral,

and the other antero-supero-medial. The lateral surface is in relation with the branches of the internal iliac vessels, including the uterine artery and vein, the main trunks themselves lying behind and somewhat below the plexus. One of these branches —usually the middle vesical—passes through the plexus to ramify upon its medial surface, supplying its constituents. The levator ani is separated from this aspect of the plexus by the parietal pelvic fascia, some fibro-fatty tissue, and the vessels mentioned above.

The medial surface is closely adapted to the lateral aspect of the ampulla of the rectum, to which it is attached by the nerves it supplies to that organ. Indeed the two plexuses may be described as clasping the rectum in much the same manner that the levator ani embraces the anal canal; for example, like the two halves of a split funnel, adherent to its lower rim. The terminal portion of the pelvic ureter crosses the superior border of the plexus from without inwards, under the peritoneum of the pouch of Douglas, to be related to its medial surface for a short distance.

As previously stated, the pelvic plexus is bilaminar, a disposition seen particularly well in dissections in infants. The constituent sheets are very closely adapted and the component fibres much intermingled, but it is easy to demonstrate the continuation of the medial sheet with the corresponding inferior hypogastric plexus, and the lateral with the branches from the sacral nerves.

With certain reservations, all the pelvic viscera are supplied almost exclusively by the pelvic plexus, a fact which accounts for its considerable size. The nerves of the uterus leave its anterior border with those to the bladder and vagina, from which they are at first inseparable; the rectal supply remains separate from the beginning. Latarjet has suggested that the nerves to the vagina and bladder appear to continue the lateral, sacral side of the plexus, those to the uterus being derived from the medial —hypogastric— lamina, but I have been unable to follow this selectivity in my dissections. The nerves to the bladder rapidly separate after a short distance, leaving the uterine nerves to course as a thick bundle within the sacro-vaginal (utero-sacral) folds. In this position they are intimately related to the contained sacro-recto-uterine ligament, together with which they run to the cervix, crossing the lateral aspect of the corresponding posterior vaginal fornix in their course, and lying medial to the crossing of the uterine artery and the ureter.

It is impossible, by gross dissection, to follow the majority

of the nerves after their entrance into the uterus, but a few fine filaments pass forwards and upwards under the peritoneal coat of that organ, upon which they can be traced for a considerable distance, before their abrupt termination in the muscularis. A separate long branch may similarly be followed along the uterine artery throughout its macroscopic course.

The uterus obtains a small but constant nerve supply from the inferior hypogastric plexus directly, without the intermediation of the pelvic plexus. This nerve, "the lateral nerve of the uterus," leaves its parent plexus at its middle, and passes horizontally forwards to its destination. It is, however, impossible to trace any separate areas of distribution of the various nerves in the uterus, as Tuskai has suggested.

A considerable amount of discussion has centered round the question of the ganglionic nature of the pelvic plexus, beginning with the historic argument between Lee and Beck in the middle of the last century. Lee,[26] Frankenhauser,[10] Jung,[27] Dalyrimple,[28] Hashimoto,[29] and Robinson,[30] described it as a definite ganglion, while Beck,[5] Kilian,[31] Körner,[32] Luschka,[20] Polle,[33] Jastreboff,[34] Pissemski,[35] Latarjet and Rochet,[36] Hovelacque,[24] and Segond,[25] have all denied the older assumption on purely anatomical lines. The question has been fairly completely settled by Dahl,[37] who confirmed the majority opinion by microscopic proof of the plexiform, rather than ganglionic nature of the structure. My own researches are in complete accord with Dahl's findings, that the plexus consists of an interlacement of nerve-fibres containing numbers of extremely small, almost microscopic, ganglia.

A good deal of this discussion has apparently been the result of the description of small paracervical ganglia by Luschka, Kehrer, Polle, Koch, Henle, and others. The presence of these structures has been excellently demonstrated recently by Gemmell,[38] who found them grouped particularly around the uterine artery. "Ganglia cervicalia uteri" do exist, but they are minute and scattered; they merely represent offshoots from the main pelvic plexus, and their name should not be confused with the same title attached by some of the older writers to the parent structure.

Histology of the Extra-Uterine System.

I have elsewhere[17] described in some detail the microscopic anatomy of the presacral nerve and as, with the exception of the nervi erigentes, the histology of the whole of the extrinsic

nerve supply to the uterus is identical with that of the component part referred to, it is unnecessary here to do more than outline its general structure. Each of the plexuses described previously consists of a series of nerve bundles lying in a fibro-fatty cellular meshwork (Fig. 4). The nerve fibres are medullated and non-medullated in varying proportion, according to the particular portion of the pathway examined. Each nerve bundle contains, at frequent intervals throughout its course, numbers of ganglion cells, typical in their morphology and reactions of sympathetic cells elsewhere (Fig. 4). These ganglion cells are of the three types classified by Cajal, and are present in great profusion, sometimes lying discretely, at others congregated into veritable microganglia. It is the presence of the latter which would appear to render futile so much of the discussion concerning the exact site of the peripheral cell-station controlling the uterine mechanism; relays may obviously occur in these ganglion cells and microganglia at any place along the very lengthy system under consideration.

The Central Connexions.

The exact anatomy of the central connexions of the uterine nerves remains obscure, as it is almost impossible in degeneration experiments to isolate the specific pathways to the organ. The centres for the efferent pathways to the pelvic organs generally lie in the intermedio-lateral tract in the lower dorsal and lumbo-sacral regions (sympathetic), and the medio-ventral columns in the sacral region (parasympathetic), the exact segmental distribution varying in different animals. Centres for the afferent pathways remain unplaced, but it is probable, on comparative grounds, that they are placed in the posterior root ganglia, as suggested by Edinger.

The Intrinsic Innervation of the Uterus.

Half a century of research by a considerable number of the most eminent authorities has failed to establish some of the most important details concerning the exact anatomy of the intrinsic nerve-supply of the uterus; but the principal sources of dissension, and the information derived in their elucidation, are of so fundamental an interest that any study cannot be complete without at least a cursory examination of their more salient features. The following bibliography summarizes the work published to-date.

Bibliography.

(*a*) *Concerning the nerve fibres themselves.*

Remak[39] was apparently the first to demonstrate histologically the presence of nerve fibres in the uterine substance. He studied them particularly in pregnant animals, and stated that they differed in the pregnant and non-pregnant uterus, being myelinated in the former and non-myelinated in the latter.

Kilian[31] stated that upon their entry into the wall of the uterus in animals the medullated nerve fibres lose their sheath, although in women the sheath is retained. He found an equal distribution of nerves throughout the uterus, with the exception of the cervix, which obtained a somewhat richer supply, and he was also able to follow individual nerves right up to the mucous membrane. During pregnancy the number of nerves was not increased.

Polle,[33] working with similar material, reported findings almost identical with those of Kilian.

Lindgren[40] described a fine plexus, composed of minute fibrils and tiny cells, in the deeper part of the mucous membrane of the os uteri.

Frankenhauser[7] found both myelinated nerves along the blood-vessels and non-myelinated fibres passing to the smooth muscle, others passing to the epithelium, sending small branches into the cells of the mucous membrane.

Patenko[41] reported findings similar to those of Lindgren and Frankenhauser. The submucosa contained a fine plexus of non-medullated nerves, from which fine fibrils were distributed to the epithelium.

Razumowski[42] similarly described a submucous meshwork supplying the decidua, and an abundance of myelinated and non-myelinated fibres in the muscularis and along the blood-vessels. He was unable to demonstrate free nerve endings of any type, and also denied that pregnancy caused either hypotrophy or multiplication of the uterine nerves.

Owsjanikoff[43] was unable to demonstrate nerve plexuses in the muscularis, and also described the entrance of the nerve fibres into the individual muscle fibres.

Bordé,[44] the first to employ the intravital methylene-blue method of staining, demonstrated the presence of the non-myelinated fibres more effectively than had been possible with the older impregnation and degeneration methods.

Herlitzka[45] used methylene-blue intra-parenchymatously to demonstrate the entrance of the nerve fibres into the muscles.

He was able to show three types of nerve in the wall of the uterus; non-myelinated blood-vessel nerves; cerebro-spinal nerves with Ranvier's nodes, ending intracellularly; and myelinate sympathetic fibres to the muscles. Each system appeared to be isolated by lack of any communication of its component nerves with those of the other systems.

Schenk[46] similarly showed nerve fibres entering the muscle bundles.

Stohr[47] was unable to demonstrate the relation of the nerves to the mucous membrane, but showed how the myelin sheath was lost when a myelinated nerve entered a muscle fibre.

Clivio[48] described intramuscular and submucous plexuses composed of many fine nerve fibrils. In addition, he found nerve-endings in the epithelium proper.

Landowski[49] demonstrated similar rich plexuses.

von Gawronsky,[50] using the methylene-blue technique, described a plexiform arrangement of the nerves in the muscularis. Although subepithelial tufts were present, nerves or nerve ends could not be seen in the epithelium itself. He was particularly impressed with the richness of the blood-vessel supply.

Kostlin[51] described the presence of a fine nerve plexus running round the lumen of the uterus, situated in the mucous membrane. Fine threads entered the epithelium, to end in buttons on the individual cells.

Lebhardt,[52] in an exhaustive investigation, demonstrated the richness of the intrinsic uterine nerve supply, and claimed to have shown cone-shaped nerve-endings in the muscle.

Acconci[53] saw nerves of some size branching out in a star-like manner beneath the epithelium, but does not discuss the nerve-endings themselves.

Hoogkamer,[54] using the methylene-blue method, was impressed by the richness of the nerve supply in the uterus. He found tree-shaped nerve-ends in the mucous membrane, and traced fine fibrils between the cells of the epithelium, but was unable to demonstrate nerves ending intracellularly.

Keiffer[55] traced the nerves accompanying the uterine blood-vessels to their termination, to find them ending either freely or in buttons upon the vascular endothelium of the capillaries. In his earlier work Keiffer claimed that all the nerves in the uterus were non-myelinated, but he has since retracted from this position.

Kolliker[56] states that the nerves are distributed with the blood-vessels, and are most profusely distributed to the cervix.

Dahl,[9] using Rougalit's supra-vital methylene-blue technique and the impregnation methods, again demonstrated the richness of the intrinsic nerve supply, both medullated and non-medullated among the muscle fibres and around the blood-vessels. The external os received fine, single, non-medullated fibres only, but the cervical musculature shared the general richness. The muscular nerves terminated without any specific type of nerve-ending other than certain cone-shaped enlargements. The same writer was also unable to find any nerve fibres in the mucous epithelium, although bundles could be traced to the mucosa. Similarly he did not find any important change in the nerves of the uterus during pregnancy.

Morrison-Lacombe[18] states that "all the nerves of the uterus form a widely meshed plexus under its peritoneal coat. The nerves leaving this plexus run at right angles right through the thickness of the uterus independent of the blood-vessels, some, according to Clivio, having a corkscrew course." The nerves of the cervix are more numerous than those of the body. The muscular branches lie in the direction of the muscle fibres, in which they terminate in free, or in button-like, endings. The mucous branches form a plexus either beneath or within the chorion, to supply the glands and epithelium. Both types of nerve are present.

La Torre,[57] using Cajal's silver hydroquinone method, is convinced from his recent researches that all the intra-uterine nerves are non-myelinated.

(*b*) *Concerning the ganglion cells.*

The question of the existence of the ganglion cells within the substance of the uterus, a problem of fundamental physiological importance, has been discused even more minutely than the preceding:

Korner,[32] Luschka,[20] Polle,[33] Koch,[58] Remak,[39] Kalischer,[59] Roith,[60] Kolliker,[56] Rohrig,[61] Ogata,[62] Dahl,[9] Gentes,[63] Toldt,[64] Sterbacken,[65] Marocco,[66] Acconci,[53] Labhardt[52] Bruckner and Mezinescu,[67] Fleming,[68] and Medower,[69] all failed to establish their presence, in spite of the most exhaustive research and the employment of a variety of staining methods. On the other hand, Kehrer,[19] and Razumowski,[42] found them in the uterine submucosa of animals; Krause,[70] and Patenko,[41] on the nerve fibres in the muscularis; von Gawronsky,[50] in the muscularis and submucosa in women and mammals; Spiegelberg,[71] Mabuchi,[72] Kollossoff,[73] Spampani,[74] and Schenk,[46] scattered in the uterine

substance, while Reimann,[75] and Rein,[21] were convinced of their presence within the uterus on physiological grounds, although they had each failed to demonstrate the fact histologically. Keiffer[55] found ganglion cells in nests, "intra-uterine ganglia," at the bifurcation of the blood-vessels, while Hoogkamer[54] saw them in great variety and greater profusion throughout the uterine substance, and suggested the presence of an extensive ganglion cell apparatus throughout both muscle and mucosa.

The findings of Herlitzka,[45] Clivo,[18] and Kostlin[51] lie somewhere between these extremes. Each of these investigators described in the mammalian and human uterus cells which, though morphologically identical with multipolar ganglion cells, remained entirely unconnected with the intra-uterine nerves. On this account these investigators did not accept these elements as true ganglion cells, but described them alternatively as "intermediate" cells (Herlitzka) or "Fadenzellen" (literally "thread-cells," Kostlin). Bruckner and Mezinescu[65] similarly found "all over the uterus, particularly in the mucous membrane and in the neighbourhood of the vessels, a great number of small cells which vaguely stain like nerve cells," and considered them to be "merely plasma cells or Ehrlich's mast-cells, which differ completely in their size, protoplasmic structure and nucleus from nerve cells." Again Dahl,[9] while expressing his astonishment at the number of writers who had described true ganglion cells in the uterine substance, admits that "in certain circumstances, as with Bielschowsky preparations, cells similar to ganglion cells can be seen while, with intravital, methylene-blue staining, cells like muscle-cells and lymph-cells may be so disguised as to be difficult to distinguish from ganglion cells."

The results of my own researches, carried out in freshly-removed operation specimens of the human uterus, stained intra-vitally and supra-vitally with methylene blue or by modifications of the methods of Cajal, Levaditi, Bielschowsky, and Prince may be summarized as follows:

Nerve fibres, both myelinated and non-myelinated, are scattered throughout the uterine substance, arising from nerve-bundles of considerable size situated at its periphery. Both sets of structures are extremely well demonstrated by the use of the supra-vital methylene-blue staining method (Figs. 5 and 6), a process often astonishing in its selectivity, but limited severely by its attendant counter-staining difficulties. In the body of the uterus the nerve fibres are found lying between, and parallel with, the smooth muscle fibres, and surrounding the capillary blood-

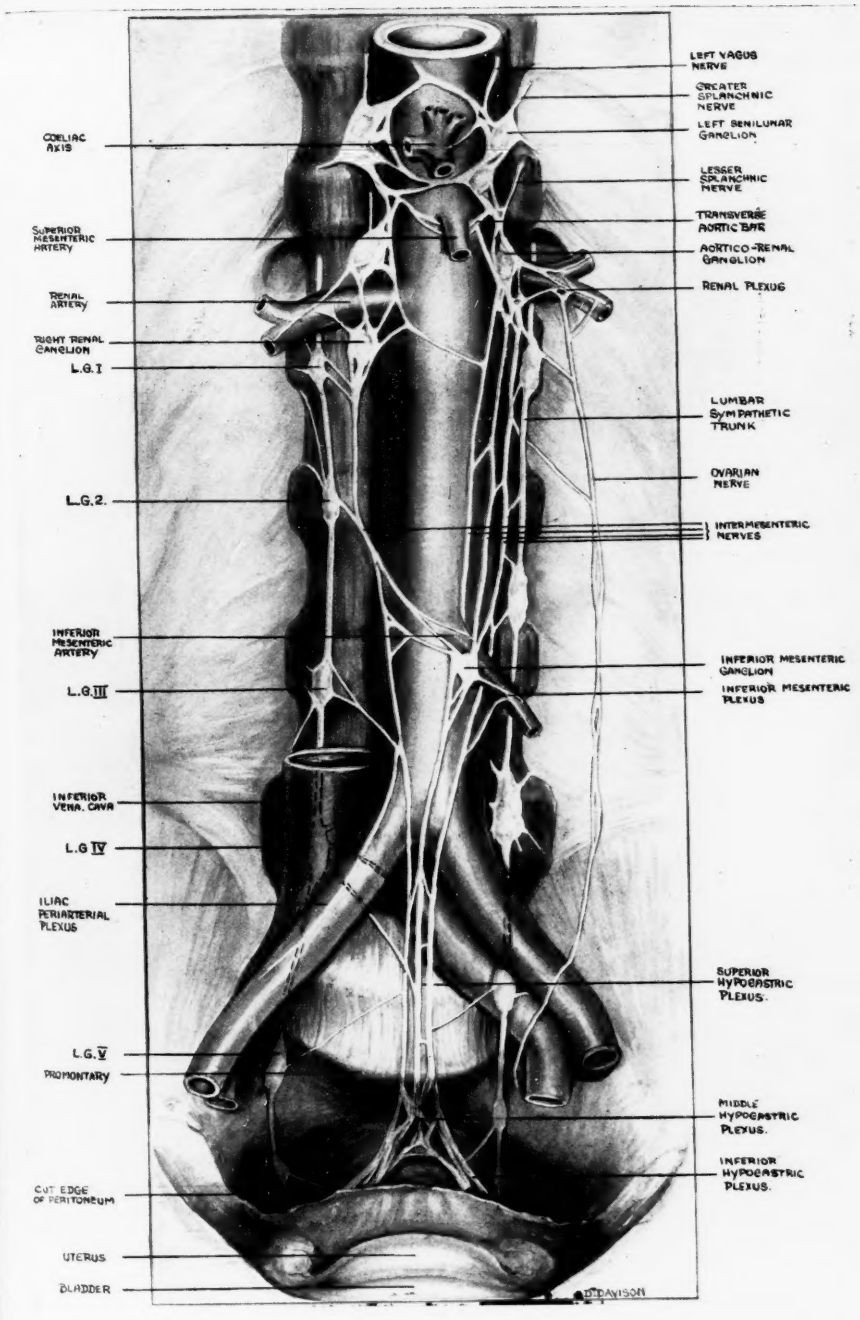

FIG. 1. The nerves of the uterus—abdominal supply.

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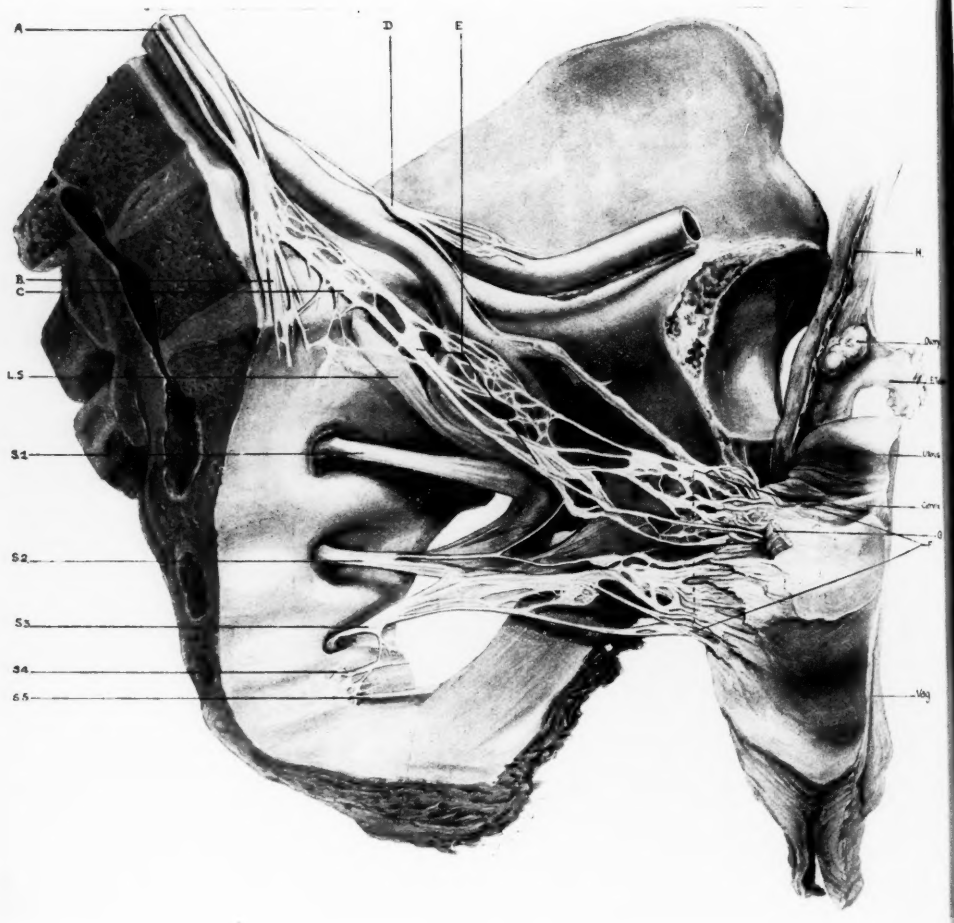

FIG. 2. The nerves of the uterus (adult)

A. Superior hypogastric plexus. B. and C. Middle hypogastric plexus (right and left divisions). D. External ilias plexus. E. Inferior hypogastric plexus. F. Plexus of Frankenhauser. G. Utero sacral ligament. H. Ovarian plexus.

FIG. 3. Low power view of the presacral nerve in transverse section. Two large and several small nerve bundles are present, lying in a fibro-fatty-cellular meshwork. (From an operative specimen, stained haemalum and eosin. ×60.)

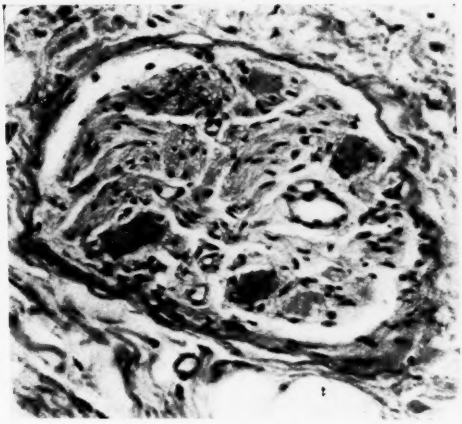

FIG. 4. High power view of a single nerve bundle in the presacral nerve. The three usual types of sympathetic ganglion cell are seen lying in a meshwork of fine nerve fibres. (Crown-cell, glomerular cell, astrocyte). The capsule is very thick, and satellite cells are present around the ? degenerated ganglion cells. (From an operative specimen, stained mercurochrome methylene-blue. ×250.)

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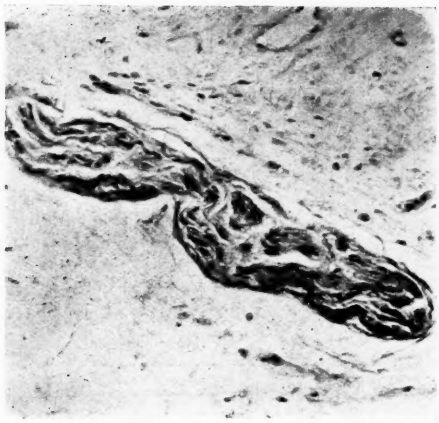

FIG. 5. High power view of a nerve bundle in the wall of the human uterus. Both myelinated and non-myelinated fibres are present. Stained supra-vital methylene-blue. × 200.

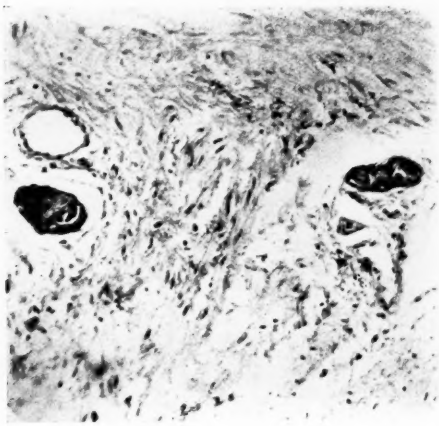

FIG. 6. Nerve bundles in the wall of the human uterus. Stained supra-vital methylene-blue. × 150.

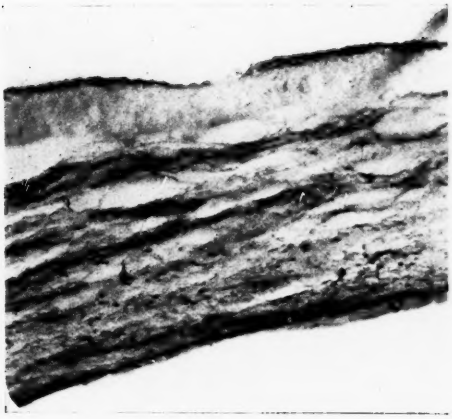

FIG. 7. High power view of the part of the wall of the human uterus adjoining the cervical canal. A meshwork of fine non-myelinated nerve fibres is seen lying subjacent to the columnar epithelium, which itself is nerveless. (The cavity on the other side is that of a Nabothian follicle.) Stained modified Levaditi. × 250.

FIG. 8. Low magnification of the human cervix uteri, to show the distribution of the subepithelial nerve plexus. The plexus is seen as a narrow dark-staining line just beneath the epithelium of the projecting portions of the cervix. The central dimple is the os cervicis. Stained erythrosin Prince. × 3.

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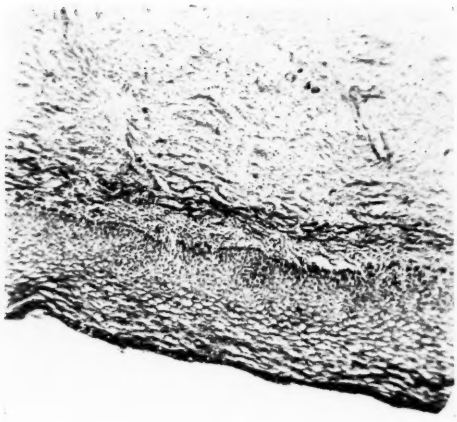

FIG. 9. Low power view of a section taken through the cervix at its most projecting part. A tangled meshwork of fine nerve fibres is seen lying directly beneath the equamous epithelium. Stained erythrosin Prince. ×60.

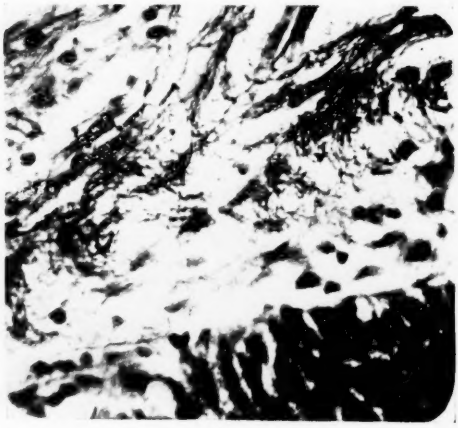

FIG. 10. High power view of Fig. 9. A nerve plexus of fine non-myelinated fibres is present, containing several tiny spider-shaped nerve cells. ×500.

FIG. 11. Low power view of a section taken through the cervix near the external os. The subepithelial plexus is absent. Stained erythrosin Prince. ×60.

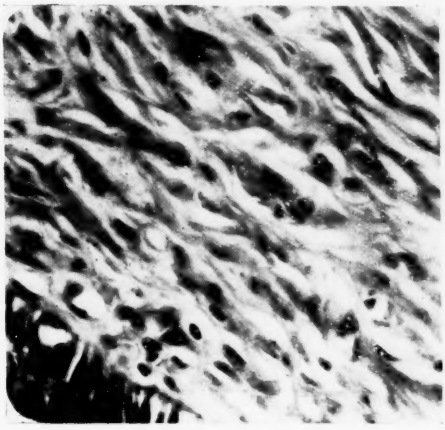

FIG. 12. High power view of Fig. 11. No nerve fibres can be seen beneath the epithelium. ×500.

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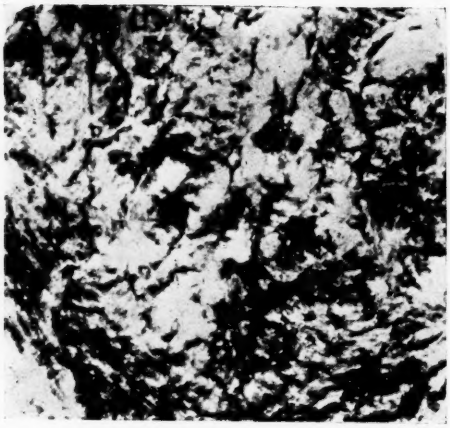

FIG. 13. Ganglion cells in the wall of the human uterus. Stained modified Cajal. ×250.

FIG. 14. A ganglion cell in the wall of the human uterus. The deep-staining nucleus is surrounded by a non-condensed area of the cell structure. (The surrounding tissue has been teased away for demonstration purposes). Stained modified Bielschowsky. ×250.

vessels. In the cervix, in addition to this situation, fine non-myelinated nerves are present just beneath the epithelium of the cervical canal (Fig. 7), and of the vaginal portion of the cervix (Fig. 9). I have never seen nerve fibres beneath the mucosa of the corpus uteri, nor have I been able to trace any nerve fibres ending within the epithelium of any part of the organ. I have similarly been unable to demonstrate any specific type of nerve-ending.

The preponderence of the uterine nerves around the capillaries appears to indicate that the main nerve supply to that organ is directed primarily to the control of these vessels, although it is by no means easy to demonstrate the termination of the nerves in the vascular endothelium. It is significant in this connexion that the vessels of the cervix are more scantily supplied than those of the body.

The subepithelial nerves in the cervix already referred to, differ in type in the two situations in which they are found. Those beneath the cells lining the internal os lie in fine, straight, parallel bundles, while the corresponding nerves below the external (vaginal) surface are highly irregular, forming a complicated plexus containing many spidery ganglion cells. This latter plexus would appear to be intimately associated with sensation, for, as is seen in figure 8, and further illustrated by figures 9, 10, 11, and 12, it is present only in those projecting parts of the vaginal cervix which my investigations have demonstrated to be the sole areas of the uterus sensitive to touch.

The ganglion cells referred to are extremely tiny, but they *are* cells and they *do* connect with the nerves of the plexus which contains them. The situation, however, in which they are found is the only part of the whole uterus in which ganglion cells occur with any degree of constancy. I have searched the corpus uteri in 300 sections through 10 specimens, and only once (Figs. 13 and 14) have I encountered what might appear to be true ganglion cells, though they are numerous outside the muscularis just beneath the peritoneum.

In view of the bulk of the opinion expressed in the literature, and of the above findings, it may be stated definitely that, with the exception of the tiny ganglion cells in the (probably) cerebro-spinal subepithelial plexus of the vaginal portion of the cervix, ganglion cells do not occur with any degree of constancy within the substance of the uterus. In any case, the importance of the problem has probably been much exaggerated, owing to failure to realize the fact that there are sufficient micro-ganglia alongside

the cervix to carry out all the mechanism necessary for "automatic" action in the separated uterus.

I am indebted to Professor J. S. B. Stopford, Department of Anatomy, for dissecting room and other facilities; to Professor D. Dougal, Department of Gynaecology, for research facilities; to Professor W. Fletcher Shaw, St. Mary's Hospital, Manchester, for laboratory facilities; and to the Dickenson Trustees, for the Scholarship which has financed the present work.

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(*The discussion on this paper will be found on page* 536.)

Hormonic Factors Controlling the Functional Activity of the Uterus.

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THE investigations of the last decade have made it abundantly clear that the mechanism of uterine action includes certain very important factors of an endocrine nature. These hormonic substances play a determining part in controlling the changes in the organ at the various stages of the sex cycle which, in the human subject, essentially connotes the menstrual cycle and pregnancy. The alterations in the uterus include changes in two main tissues which differ functionally, namely the endometrium and the muscle. In the former cyclical growth and destructive processes occur, while, in certain circumstances, the development of a specialized tissue for the protection and nutrition of the embryo may take place; in the muscle, too, growth and involution form part of the cyclical changes, but, in addition, alterations in the activity and reactivity of the uterine muscular system play a very important part in determining the physiological activity of the uterus. The endometrial and muscular changes are, of course, very closely correlated in association with the functional activity of the organ.

The functional importance of the activity of the muscle has been known to clinicians for many years. The increase in the rhythmic contractions during the course of pregnancy is of recognized importance in diagnosis; the inactve uterus at parturition has ever been the despair of obstetricians; and the control of the over active organ with the resultant pain may often present a serious problem. These few examples merely emphasize the need for an understanding of the factors which control uterine contractions and contractibility and, also, of the relation of the latter processes to the activity of the organ as a whole.

The uterus shares with other unstriated muscles the property of being affected by minute doses of certain drugs, and it exhibits a specific response to very small doses of an extract of the

posterior pituitary lobe containing the oxytocic hormone. The response is, however, by no means constant and the variations in the sensivity of the muscle afford a valuable criterion of its general reactivity. The sensitivity has in fact been found to alter in a definite manner during the various stages of the sexual cycle and to be under the control of ovarian hormones.

ALTERATIONS IN THE REACTIVITY IN THE HUMAN SUBJECT.

That the human uterine muscle undergoes periodic changes in reactivity during the menstrual cycle was shown by Knaus,[1] who determined the effects of pituitrin upon the organ *in vivo* by direct registration of the contractions. Knaus found that during the first half of the cycle the intramuscular injection of pituitrin was followed by contraction of the uterus, while later on the drug had not any effect on the uterus. The onset of menstruation coincided with a return of the reactivity to the oxytocic hormone. Since the absence of the uterine reactivity occurred during that part of the cycle when the corpus luteum was present in the ovary, and presumably exerting its secretory activity, it appeared quite likely, as Knaus suggested, that a luteal secretion was responsible for inhibiting the reactivity of the uterine muscle.

During pregnancy the *in vivo* method of investigation is, of course, impossible, but the uterine activity may be determined by investigating the properties of uterine muscle removed at operation. The latter method has indeed the advantage that it enables very accurate quantitative results to be obtained (which is difficult with the *in vivo* method) and, moreover, secondary effects on the uterine muscle such as may, for example, result from alterations in the vaso-motor system are eliminated.

The investigation of the human uterine muscle made on material (placed at my disposal by Professor Johnstone, Dr. Young, Professor Hendry and their assistant, to all of whom I am greatly indebted) removed at the various stages of pregnancy has yielded certain very well-defined results. It was found that during the early stages of gestation either the muscle was not affected at all by the oxytocic hormone, or comparatively large doses of the drug had to be used before a contraction could be obtained. Vaso-pressin, on the other hand, always caused a contraction even in those cases in which oxytocin remained ineffective. Thus in the earliest specimen received, removed from a pregnancy of two months' duration, large doses of oxytocin did not have any effect whatever, while the pressor hormone caused a contraction. As pregnancy proceeded the dose of oxytocin

necessary to bring about contraction gradually decreased, until ultimately, uterine muscle removed actually during parturition responded to very small doses of the hormone. There were variations between the different uteri examined suggesting that the reactivity at one particular stage of pregnancy is not necessarily fixed; but on the whole it appeared that parturition represented the highest stage of reactivity of the uterine muscle. It may also be added that in a few cases of strips removed from the lower uterine segment at labour the muscular reactivity was decidedly lower than that of strips removed from the body of the uterus at the same stage.

This sequence of changes in uterine reactivity is highly specific and the reactions of the uterus to a number of other drugs do not undergo similar alterations. At the same time oxytocin is not the only substance of which the action on the uterine muscle varies with the sex cycle, for it was found that the effect of ergotoxin exhibited similar variations. Strips of human uterine muscle removed during the various stages of pregnancy were, with few exceptions, not effected even by larger doses of ergotoxin, while very small doses (i.e. in concentrations of 1 in 10^7 to 1 in 3×10^7) sufficed to cause marked contractions of muscle removed at parturition.

These findings obtained with oxytocin and ergotoxin during pregnancy suggest that the uterine muscle contains a receptive system (muscular or neuro-muscular) which undergoes definite variations in its reactivity to specific substances during the sex cycle. And such a conclusion gains support from the observations of Hasama,[2] who showed that the response of the rabbit's uterus, as determined by the electrical changes, to stimulation of the hypogastric nerve is qualitatively different in the pregnant and non-pregnant animal; for in the latter a motor effect is apparently obtained, while during gestation inhibition seems to be the chief effect.

The elucidation of the hormonic factors responsible for the changes in reactivity has been based mainly on animal experiments, and it is therefore necessary to refer briefly to corresponding phenomena in the rabbit during the various stages of the sex cycle. In that animal an active corpus luteum occurs under two conditions, namely, (1) pregnancy and (2) pseudo-pregnancy. The latter period representing as it does a phase of luteal secretion in the absence of gestation, therefore corresponds functionally to the second part of the menstrual cycle in primates, when it appears likely that the corpus luteum is also active. Again, just as in primates this stage is characterized by specific altera-

tions in the endometrium representing the secretory stage, so also in the rabbit the uterine endometrium shows alterations which are typical (progestational proliferation). Moreover, the uterine muscle of the rabbit during pseudo-pregnancy exhibits the same lack of reactivity to the posterior lobe hormones as characterizes the corpus luteum phase in the human menstrual cycle.

The changes in the uterine muscle of the rabbit during pregnancy show a remarkable similarity to those observed in the human subject. During the first half of gestation (corresponding in duration to pseudo-pregnancy) the uterine muscle does not react either to oxytocin or to vaso-pressin. This is succeeded by a stage in which the pressor hormone causes contraction of the muscle while oxytocin has no effect. Still later in gestation the reactivity to the oxytocic hormone returns; at first comparatively large doses are necessary to cause contraction, but as pregnancy proceeds the effective dose becomes smaller until, ultimately, at parturition very small amounts of oxytocin produce contraction of the uterus. It is a remarkable fact that not only does the sequence of reactivity changes in the rabbit and human uterus coincide, but also the effective amounts of the hormone at the various stages are practically equivalent. Thus, for example, in the rabbit the parturient uterus reacts to a dose of 0.001 to 0.01 units of oxytocin in 100 cubic centimetres of solution, while the corresponding dose for the human uterus is 0.003 to 0.01 units.

During the early stages of the puerperium the reactivity of the rabbit's uterus to oxytocin decreases very rapidly, and by the fifth day after parturition, before involution is completed, the effective dose of the hormone may have increased by 100 times. Thus, parturition truly marks the apex in the reactivity curve of the uterus. Investigations of the puerperal changes in the human organ are at present being conducted by Dr. Steere at the Royal Simpson Hospital in Edinburgh and the preliminary results suggest that in the human subject, too, a fall in the reactivity to oxytocin follows labour.

At present two ovarian hormonic factors are known to affect the reactivity of uterine muscle and these probably control the cyclical changes described above: they are (1) oestrin, and (2) a hormone secreted by the corpus luteum.

In 1926, Bourne and Burn[3] showed that the addition of a preparation containing oestrin to the solution in which a horn of a guinea-pig's uterus was suspended markedly increased the reaction to oxytocin, and these workers therefore concluded that

oestrin could sensitize the uterine muscle to oxytocin. Subsequent investigations by means of the same method, i.e. on the isolated uterus of the guinea-pig (Jeffcoate,[4] Illingworth, Marshall and Robson[5]) have shown, however, that the sensitizing action is not due to oestrin and may be obtained by means of a variety of urine preparations which do not contain this hormone. Quite recently Marrian and Newton[6] have, again using the *in vitro* method, claimed that oestrin on the contrary diminishes the reaction of the guinea pig uterus to oxytocin. In this investigation, however, the doses used were much greater than those found in the blood under physiological conditions and it is, thus, not yet clear whether the effect is of physiological importance. It has, on the other hand, been very clearly demonstrated that oestrin can markedly increase the reactivity of the rabbit's uterus when the hormone is acting *in vivo* (author's unpublished observations). For when pure oestrin (trihydroxy-oestrin, British Drug House) is injected into rabbits a definite effect is observed and the uterine reactivity to oxytocin is always much greater after the injection than before it, so that there appears to be no doubt that under these conditions (i.e. *in vivo*) oestrin very markedly increases the sensivity of the uterus. It may be added that a fairly prolonged period of injection may be necessary before the high reactivity is obtained. Moreover, the reactivity of the uterus to oxytocin after the injection of oestrin may be of the same order as that observed at parturition when the uterus reaches its maximum reactivity in the cycle.

As regards the endocrine activity of the corpus luteum it is now well established that this structure secretes a substance which produces specific changes in the endometrium. In the rabbit these changes consist in a typical proliferation which has been called progestational proliferation because it is characteristic of the pregnant and pseudo-pregnant uterus.[8] In primates the secretory phase[9] observed during the second half of the menstrual cycle is also brought about by a luteal hormone. Now, the corpus luteum also produces a hormone which exerts an action entirely opposite to that of oestrin on uterine reactivity. This was definitely shown by Knaus[10] when he injected an extract of the corpus luteum into rabbits and found that the uterine reaction to oxytocin was thereby abolished.

It was at first suggested that the luteal secretion responsible for the endometrial changes also acted upon the muscle, producing inhibition of the reactivity to oxytocin. Later work[11, 12, 13, 14, 15] suggests that this is probably not the case, and that the inhibitory

phenomenon is dependent upon a specific luteal secretion, different from that which acts upon the endometrium. This substance might conveniently be called "the inhibitory hormone" of the corpus luteum.

The typical progestational luteal action on the endometrium cannot take place unless a certain quantity of oestrin is present. This fact was demonstrated in the first instance by Allen[16] and by Hisaw and Leonard[17] in the rabbit; but it also applies to the primates in which the luteal effect can only be produced on a uterus previously prepared by oestrin,[18] and the experiments of Kaufmann[19] have lately demonstrated that in the human subject, too, the action of the luteal hormone on the uterus previously treated with oestrin causes a typical premenstrual condition of the endometrium and leads to menstruation.

The same kind of relation between these hormones also holds for their action on the uterine muscle, for the inhibitory hormone of the corpus luteum is also unable to exert its action in the absence of a certain requisite quantity of oestrin. Moreover, the amount of oestrin necessary for the effective action of the inhibitory hormone is larger than the quantity required for the endometrial effect of the proliferative hormone. Thus, under certain experimental conditions[21] it is possible to induce the typical progestational effect in the rabbit's uterus without inducing the inhibitory action; if the amount of oestrin is increased then both the endometrial and muscular effects result. On the other hand, large amounts of oestrin are unable to over-ride the action of the inhibitory luteal hormone.[11]

Thus, although oestrin increases the reactivity of the uterine muscle, yet oestrin together with the inhibitory hormone brings about inhibition, and is in fact essential for the development of the inhibitory reaction. It will naturally be asked what are the respective functions of oestrin and the inhibitory luteal hormone in determining the changes in reactivity which occur during gestation, and to what extent these two hormones are responsible for the maintenance of pregnancy and initiation of parturition. Any attempt at explanation of this problem must necessarily take into account the fact that in the human subject the ovaries can apparently be removed at an early stage of pregnancy without interfering in any way with the subsequent normal development of the foetus or with parturition. (See cases collected by Ask-Upmark.[23]) This fact cannot be explained by assuming that the luteal hormones may be produced in other parts of the body since, with the single exception of one case reported by Mazer and

Goldstein[24] observers are agreed that other tissues, and the placenta in particular, do not contain these hormones.[25, 26] If, therefore, the changes in uterine reactivity play an essential part in controlling pregnancy and parturition, then they must, after the earliest stages of gestation, develop independently of the corpus hormones of the corpus luteum, and hence the gradually increasing reactivity observed during pregnancy cannot be due merely to the withdrawal of the luteal secretion. Such a conclusion is supported by the finding that parturition is rapidly followed by a fall in the uterine reactivity, although the luteal secretion must by then have completely ceased. All these considerations make it seem more likely that the increase in the sensitivity of the reactive system of the uterus during the course of gestation results from the effects of some active factor, and the experiments with oestrin described above suggest that this ovarian hormone, the production of which continues after removal of both ovaries[27] presumably by the placenta, may be largely concerned in effecting the increase in reactivity. The fact that both the oestrin content of the blood and its excretion in the urine gradually increase during gestation, reach a maximum at parturition and, thereafter, rapidly decrease following expulsion of the placenta,[28, 29] thus, undergoing alterations similar to those characteristic of uterine reactivity, supports the hypothesis that these two parallel series of changes are causally related.

The expenses of the original investigations described by the author in this communication were, in part, defrayed by a grant from the Medical Research Council.

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An Analysis of 937 Cases of Post-Menopausal Haemorrhage.

BY

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VAGINAL haemorrhage occurring in a woman who has passed the time of the menopause has for many years been regarded as a condition that does not admit of any delay in diagnosis and, from time to time, statistics have been published dealing with the aetiological factors. In nearly all such reports the statement is made that malignant disease in some part of the genital tract is the origin of the bleeding in the majority of cases.

It may be of interest, therefore, to place on record the results of a statistical survey of a series comprising a much larger number of cases than that usually reported.

At a recent meeting of the Edinburgh Obstetrical Society a discussion on post-menopausal haemorrhage led to the presentation of series of cases by seven different observers; and the present analysis has been made from the figures obtained from these different sources. Out of the total of 937 cases 180 were taken from private records, the remainder were obtained from the records of hospital clinics in both Edinburgh and Glasgow.

For the purpose of the investigation, all cases in which bleeding was noted have been included, not only those in which the symptom complained of was haemorrhage. In some the bleeding was a slight spotting only, in others it was profuse. The determination of the time of the menopause was found in many instances to be most difficult, and it was taken, therefore, that at least six months amenorrhoea was essential. In the great majority of the patients there had been a full year's freedom from vaginal loss, in a few a full year had not elapsed since the last monthly period.

The investigation has not brought to light anything to alter the view that malignant disease in the genital tract is a frequent source of post-menopausal haemorrhage. The axiom, therefore, that all such cases should be fully investigated receives the strongest support.

The analysis here presented does, however, show clearly that benign conditions are casual factors in a large number of cases—indeed in this whole series they outnumber those in the malignant group.

Of a total of 937 cases, the benign conditions operated in 533 (56.88 per cent), and the malignant in 404 (43.12 per cent).

This high proportion of non-malignant causes is, perhaps, the most interesting feature of the analysis. I am unaware of any other published figures which show a similar ratio between these two all important groups. The large total of 937 cases cannot be held to explain this point, for, as I shall show, the smaller groups supplied by seven different clinicians show similar proportions between the benign and the malignant. Nor can it be argued that the inclusion of cases with "mere spotting" raises the figure of the benign group, for even malignant disease may be present though the bleeding is scanty to a degree. In the recent article on Post-menopausal Bleeding, by Kanter and Klawans,[1] malignant conditions were held to be responsible in 68.4 of 98 cases, benign conditions in 31.6 per cent; i.e. malignant disease was twice as common as the non-malignant. Yet, in that article, the authors state that in 16 cases of carcinoma of the cervix the haemorrhage was "spotting" in type. If one were to consider separately those cases in which the menopause had been established for a period of at least five years, I have little doubt that the malignant group would predominate; but, from the clinical point of view, importance must be attached to bleeding at any time after cessation of the periods owing to the prevalence of cervical carcinoma.

Table I. In this table I have placed the various aetiological factors in their order of frequency. The table shows that carcinoma of the cervix is much the most frequent cause of bleeding. It alone accounts for one-quarter of the total, and its incidence is almost twice that of the second commonest condition. In the article by Kantar and Klawans referred to, carcinoma cervicis was responsible in 52 per cent of their cases, while 50 per cent is the figure given by Tietze and C Mayer[2] in their paper on "Haemorrhage in women over 50 years of age." These figures are twice as high as that in Table I, but though the total number in each series was much smaller than ours, yet we agree in that cervical carcinoma heads the list. This is in accord, I think, with the views of most gynaecologists.

Before discussing Table I further, may I draw your attention to Table II.

TABLE I.

Order of Frequency of Various Causes.

Benign	533;	56.88 per cent
Malignant,	404	43.12 per cent

	Number of cases	Percentage
1. Carcinoma of cervix uteri	241	25.72
2. ? Ovarian dysfunction, diagnosis doubtful	141	15.05
3. Polypus: mucous and fibro-adenomatous	114	12.17
4. Carcinoma of corpus uteri	93	9.82
5. Prolapse: genital (with or without friction ulceration)	86	9.17
6. Fibromyoma and fibroid polypus: uterine	64	6.83
7. Cervicitis and vaginitis	40	4.27
8. Ovarian neoplasm: malignant	32	3.52
9. Caruncle of urethra	27	2.88
10. Senile endometritis	20	2.13
Ovarian neoplasm: benign	20	2.13
11. Carcinoma of vagina	12	1.28
Vaginal ulceration due to pessary	12	1.28
12. Carcinoma of vulva (labium)	10	1.07
13. Sarcoma of uterus, corpus, fibroid and retroperitoneal	8	0.85
14. Carcinoma of clitoris	3	0.32
15. Carcinoma of urethra	2	0.21
Prolapse of urethra	2	0.21
Tuberculous endometritis	2	0.21
Myxo-fibroma of vagina	2	0.21
Hyperpiesis (constitutional, e.g. cirrhosis of liver)	2	0.21
16. Sarcoma in cervical stump	1	0.11
Carcinoma of peritoneum (secondary to breast tumour)	1	0.11
Malignant papilloma of bladder	1	0.11
Tuberculous granuloma of urethra	1	0.11
Total	937	99.98

TABLE II.

Total cases 937

Proportion of Benign to Malignant Cases in the Seven Reported Series.

Series	Benign	Malignant
A	58.7 per cent	41.3 per cent
B	56.0 ,,	44.0 ,,
C	57.5 ,,	42.5 ,,
D	55.0 ,,	45.0 ,,
E	55.0 ,,	45.0 ,,
F	53.3 ,,	46.7 ,,
G	65.4 ,,	34.6 ,,
Average	56.88 ,,	43.12 ,,

This table sets out the ratio of benign to malignant causes in each of the seven series reported at the Edinburgh Obstetrical Society meeting in February, 1933 which form the basis of this paper.[2] It will be observed how similar are the figures in each series: the similarity is surely very remarkable. In each the benign conditions predominate. Series G was supplied by myself and consisted of a small group; this probably accounts for my figures differing from the rest, but it emphasizes, perhaps, the value of considering a large number of cases when endeavouring to arrive at a true and just conclusion.

Referring again to Table I, it will be seen that the second commonest condition is labelled "Ovarian dysfunction, diagnosis doubtful." This needs some explanation. This group includes all cases termed variously in the different series collected as: undiagnosed, fibrosis uteri, local cause absent, hyperplasia of endometrium, metropathia, and diagnosis doubtful. The very use of these expressions, and I think most of us at times have employed them, serves to show that the true cause of post-menopausal bleeding in certain instances is difficult to affirm. The important point for the clinician has been that malignant disease was not detected. Perhaps it is correct to say that in very many cases the diagnosis is in doubt, while in some the ovary is almost certainly responsible.

A study of this group leaves one not a little confused. In some the uterus is small, in others enlarged; in some the endometrium is hyperplastic, in others atrophic or apparently absent; in some the glands of the mucosa are cystic, in others the glands are small. Nor does there appear to be any constant relation between cystic glands and a thick mucosa, for even in

scanty scrapings from a curettage large cystic glands have been found, and the size of the uterus has given little clue as to the state of the endometrium it contained. The presence of follicular cysts of the ovaries has been noted in some instances, but because surgical removal of the organs has seldom been performed, the opportunities for histological study have been very limited. For these reasons, these cases have been grouped under the heading of "Ovarian dysfunction, diagnosis doubtful." Some are probably in the nature of the condition we now call "Metropathia haemorrhagica," but by no means do they all come under this category.

In most of the cases showing endometrial hyperplasia, the patient was within a few years of the menopause, and this would lend support to the view that ovarian activity was responsible for the uterine bleeding; but in one case, the patient was aged 70 years yet the curette revealed profuse scrapings containing many cystic glands, the uterus was not appreciably enlarged, and the ovaries were not felt to be cystic.

It is possible that the bleeding in some cases in which a local cause could not be discovered had a constitutional origin, such as high blood-pressure; but in the whole series of 937 cases hyperpiesis was stated only twice to be the aetiological factor. Perhaps case-notes have been at fault, but in many cases notice has been taken of the fact that the blood-pressure was not raised.

Uterine polypi form a large group in this analysis, and one cannot help feeling that, even in post-menopausal cases, mucous polypi in the uterus may have some relation to ovarian activity.

The onset of the menopause is judged clinically, in the main, by the cessation of menstruation; but we cannot yet state at what later date the ovaries cease to exert control over the uterus, nor when the ovaries cease to respond to influences derived from the other endocrine organs, e.g., the pituitary gland.

It is difficult to understand why a mucous polypus should arise in the small uterus of a patient, 10 to 12 years after the menopause, unless one accepts the theory of endocrine influence. It is certain that infection is not the stimulating factor, and the uterus, *per se*, is surely not to blame.

From Table I, genital prolapse would appear to be a factor of importance in the production of haemorrhage even in the absence of evidence of ulceration due to friction. Perhaps mere congestion may be an explanation, but constitutional or other causes may be determining factors. Generally speaking post-

menopausal haemorrhage due to prolapse is only slight in amount.

One other group may be mentioned, that of ovarian neoplasms. Among the malignant tumours are included granulosa-celled tumours, of which there were three examples, each being associated with a hyperplastic endometrium. But endometrial change is by no means a necessary prelude to vaginal haemorrhage associated with malignant ovarian neoplasms. In many instances the uterus does not show any thickened mucosa and the uterine wall is free from malignant invasion.

Benign ovarian tumours, to the number of 20, form a definite group in the analysis. With some of these torsion of the pedicle had occurred, but only in a few instances. Dermoids, fibromata, papillomatous and pseudo-mucinous cysts are all represented in the number given.

In Tables III and IV the malignant and benign cases have been listed separately. In the former, carcinomata of the cervix and body of the uterus account for 82 per cent; while in the latter doubtful cases and uterine polypi account for 47 per cent.

In conclusion, it may be stressed that the character of the haemorrhage bears little or no relation to the underlying condition. In both malignant and benign cases the bleeding may be slight or free in amount; it may have been of short duration or have lasted for weeks or months; it may, or may not have been associated with the passage of clots.

TABLE III.

Malignant Cases.

	Number of cases	Percentage
1. Cervix uteri (carcinoma)	241	59.65
2. Corpus uteri (carcinoma)	93	22.77
3. Ovary (neoplasms)	32	8.17
4. Vagina (carcinoma)	12	2.97
5. Vulva (carcinoma)	10	2.47
6. Corpus uteri (sarcoma)	8	1.98
7. Clitoris (carcinoma)	3	0.74
8. Urethra (carcinoma)	2	0.49
9. Cervical stump (sarcoma)	1	0.25
10. Peritoneum (carcinoma)	1	0.25
11. Bladder (malignant papilloma)	1	0.25
	404	99.99

TABLE IV.
Benign Cases.

	Number of cases	Percentage
1. ? Ovarian origin (diagnosis doubtful) -	141	26.45
2. Polypus: mucous and fibro-adenomatous -	114	21.39
3. Prolapse - - - - - -	86	16.13
4. Fibromyoma and fibroid polypus - -	64	12.00
5. Cervicitis and vaginitis - - -	40	7.50
6. Urethral caruncle - - -	27	5.06
7. Senile endometritis - - -	20	3.75
8. Ovarian neoplasm - - -	20	3.75
9. Pessary ulceration - - -	12	2.25
10. Prolapse of urethra - - -	2	0.38
Tuberculous endometritis - -	2	0.38
Vaginal myxo-fibroma - - -	2	0.38
Hyperpiesis - - - -	2	0.38
11. Tuberculous granuloma of urethra -	1	0.19
	553	99.99

But this much can be stated, that a fairly constant, moderate haemorrhage extending over many weeks is probably, though not necessarily, of malignant origin.

The analysis has been compiled from tables prepared in Glasgow by Professor Hendry and in Edinburgh by Professor Johnstone, Dr. Young, Dr. Haultain, Dr. Miller, Miss Herzfeld and myself. I am most grateful for the permission to make use of all their figures.

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(*The discussion on this paper will be found on page* 537.)

Fundal Rupture of the Pregnant Uterus.

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A CASE of complete fundal rupture of the uterus which was admitted recently to the Birmingham Maternity Hospital, is of some interest, as a rare form of abnormal action of the uterus.

The patient was 29 years of age and was in the thirty-sixth week of her second pregnancy. The first pregnancy had ended in a normal labour at term 18 months previously, labour had lasted 12 hours and the child was of average size. During the puerperium the patient had slight rise of temperature but got up on the tenth day and continued to lose slightly for five weeks. At the end of this time the patient was admitted to another hospital where her uterus was explored and curetted on the assumption that there might be some retained products of conception. Placental tissue was not found and the thickened endometrium was not examined microscopically. Intra-uterine injections of glycerine were given for a week, after which the bleeding ceased.

The second labour had started 24 hours before admission. The midwife in attendance sent for medical help after 12 hours because the painful and unusually powerful uterine contractions did not cause any advance of the child. The doctor watched the patient for four hours and then, since progress was not apparently being made, sent her into hospital, confident that there was no sign of shock while he had the patient under observation.

On admission. The condition of the patient was good, temperature 98.8 F., pulse-rate 110, blood pressure 130/75. The uterus was the size of 36 weeks pregnancy, which corresponded with the date estimated by the patient. The position of the head was right occipito-anterior and it was engaging in the brim of the pelvis. The foetal heart rate was 130 and uterine contractions were

infrequent and weak. On vaginal examination the os would admit two fingers, the cervix was thin, and the membranes intact.

The urine contained a light cloud of albumin but was otherwise normal. The pelvic measurements were as follows: interstitial 10½ inches, intercristal 11½ inches, external conjugate 7¾ inches.

Weak pains continued through the day and the condition of the patient remained good. Twelve hours after admission the patient began to complain of constant, dull epigastric pain, but all that could be discovered to account for this was a distended transverse colon. The foetal heart could not now be heard.

Sixteen hours later uterine contractions were stronger and the patient was becoming distressed. The head of the child was now well down in the pelvic cavity. Epigastric pain was still severe. A quarter of a grain of morphia was given.

Four hours later palpation of the abdomen showed an irregular tender mass in the epigastrium, above the uterus. The patient's condition was now definitely worse. A general anaesthetic was given and a hand introduced into the uterus: the os was now three-quarters dilated, and it was found that the fingers could be passed into the peritoneal cavity through a rent in the fundus, in which the foetal trunk was tightly gripped.

The abdomen was opened in the mid-line below the umbilicus, and the unusual condition of a uterus ruptured across the top of the fundus was discovered, a macerated foetus being partially extruded into the peritoneal cavity. There was not any free blood in the peritoneum, but a little meconium stained fluid.

Subtotal hysterectomy was performed, leaving the child, so far as possible, in the same position, and the abdomen was closed, a drainage tube being inserted. The patient made a good recovery and left the hospital three weeks later. The Wassermann reaction was negative.

As there was no obvious cause for a rupture in such an unusual position, sections of the uterine wall were taken at the edge of the rupture, with sections from the healthy part of the uterus as a control. These sections were examined by Professor Haswell Wilson, of the Birmingham University Pathological Department, whom we wish to thank for his report, of which the following is a summary:

1. On the inner wall of the uterus, at the site of rupture, is a piece of partially necrotic decidual tissue which is in an advanced state of organization.

2. The muscle fibres in this area do not stain so well as those from the healthy one. Between them is much recent haemorrhage.

There is an abnormal amount of fibrous tissue, especially in the inner part of the wall.

3. Organisms cannot be found in sections stained by Gram's method.

4. Thrombosis of the vessels in the uterine wall with commencing organization of the clot.

5. In frozen sections stained with Sudan III, evidence of fatty degeneration of the muscle fibres is wanting.

Professor Wilson does not agree with our original suggestion, namely, that the rupture was due to scarring of the uterine wall following a perforation during the exploratory curetting after the first confinement. He thinks that the predisposing cause was a myometritis occurring as a result of the infection of a retained decidual fragment, leading to fibrosis and weakening of the uterine wall at the spot. It is impossible to say whether the infection was blood borne, or whether it occurred at the first confinement, or was due to the subsequent curetting.

(*The discussion on this paper will be found on page* 537.)

Normal Labour and its Anomalies—
The Dividing Line.

BY

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WITH respect to the problems concerning which obstetricians may differ, all are agreed that normal labour performs two distinct acts. First it converts the cavity of the uterus and the vaginal passage into a single utero-vaginal sleeve, and secondly the uterus, aided by the bearing down efforts of the mother, expels the child.

Immediately prior to labour, section of the uterine wall reveals that its musculature does not present at any point striking differences in thickness from that of the organ as a whole. The external os is the only part unsupported by muscle.

The appalling results which attended *accouchement forcé* in days gone by, are well known as is, in the present day, the more general recognition of the lower uterine segment as an essential middle segment of the completed birth sleeve. These two acknowledged facts have focussed attention on one important fundamental, namely that dilatation of the cervix is not a mechanical process alone.

It is only necessary to remember that during labour the cervix becomes thinned out and elevated towards the abdomen, thereby creating more room in the pelvis.

Before the commencement of labour the walls of the uterus are, like those of any other hollow organ, of almost equal thickness throughout. Many agents exist which can, and often do, bring about anomalous uterine activity.

The commonest anomaly is expressed by a succession of spasmodic contractions which require to be repeated over a period of time before definite effects are noticeable.

Between, therefore, two widely different acts, the one co-ordinate and designed to evacuate the uterus, the other inco-ordinate and expressed by repeated acts of compression, there are innumerable varieties of uterine activity which lean now towards the co-ordinate, and now towards inco-ordinate. Perhaps the principal causes leading to inco-ordination are psychic disturbances from the higher centres, and hormonic disturbances which have for the most part accumulated from the time of puberty, but which are, as yet, imperfectly understood. To these must be added mechanical interference and oxytocic drugs.

Amid all these elements which tend to distort the normal, is there any one of greater potency which predisposes to the normal? The answer is in the affirmative, namely a presenting part, or pole of the child, which accurately fills the cervix during the whole period of formation of the utero-vaginal sleeve. It is interesting to note that the most successful part in this respect is a prolapsed arm and shoulder which together form so perfect a wedge that the cervix is sometimes lifted to quite exceptional heights in the abdomen.

When a well-fitting dilator is present the cervix and body of the uterus act in sympathy with one another, and there results that co-ordinate physiological act which we call, for short, "dilatation of the cervix."

The literal acceptance of this law of the uterus enables one to examine normal labour on the one hand, and its anomalies on the other from a singular point of vantage. In effect, a classification can be drawn up which is a constant source of help, and I would add restraint, when one is confronted with a bedside problem.

The classification has its origin in the word "sympathy," by which is meant that the one irreplaceable ingredient of normal labour is sympathy of action, or co-ordination between the cervix and the body of the uterus.

Labours at once fall into two categories, those in which sympathy exists, and those in which it is relatively, or completely, absent. In the first group, in which sympathy is present, the results will show themselves in terms of speed. We thus have slow, medium, and precipitate labours.

It is clear on reflection that this sympathy of action is the all important element. Mere strength of contractions in its absence can produce only uterine discomforture expressed by increasing tenseness, foetal distress, or rarely rupture of the uterus.

Lastly, in this first group, the one alternative to spontaneous

delivery is a condition which Fitzgibbon[1] has rightly named "uterine failure." The advantage of such a term is that it is completely accurate and, furthermore, that it signifies a condition which demands assistance if delivery is to be completed satisfactorily.

In group two in which sympathy is partly, or completely, absent three conditions are present, of which one or all may be encountered in a single labour. They are false labour, spasm of the uterus and active retention of the foetus. The latter term, for which we are indebted to Eardley Holland[2] is more indicative of the clinical facts than the term contracting ring.

I include the condition of false labour only because it so very closely precedes the true onset of labour pains with which it may be confused. To consider next spasm of the uterus and active retention of the foetus.

Perhaps the first thing which mention of these conditions brings to mind is the memory of major obstetrical procedures accompanied by trauma, and often followed by sepsis and mortality.

In fact, both these conditions exist in an early, elusive, and mild form, and as such they are of common occurrence. What is of even greater importance is that they are also innocuous to either mother or child if recognized early and treated suitably.

To take an example.[3] Disregarding type or age for the moment. If a patient commences labour, and it is found that after 24 or more hours the membranes have ruptured, that the cervix admits but two fingers, and that meconium-stained liquor amnii is coming away, it is a gross inaccuracy to think of, or refer to, the case as an example of uterine inertia. The single fact that there is evidence of foetal distress should preclude this diagnosis. How often has the labour-ward sister remarked, in such a case, "The patient is not having real pains." In making this statement, the sister states what in fact is the truth. The case is one of inco-ordinate labour lacking sympathetic action between the cervix and body of the uterus.

The only way in which the example just mentioned differs from the textbook description of spasm of the uterus, is in the severity of symptoms, and I think most of us have seen such a case pass on into obvious spasm either in course of time, or as the result of oxytocic drugs being given.

I have never adopted early radical measures for these cases, but wish to emphasize their inco-ordinate nature, and when sedative drugs, sleep, and a simple enema have been given

their trial, I am in favour of subjecting the case either to version or Caesarean section before the prospects of viability for the child have been too severely compromized.

To sum up, I lay little importance on the length of labour provided that physiological advance is being made. If, on the other hand, obvious signs of foetal distress supervene with increasing tenseness and a lack of the normal pyriform outline of the uterus. If the dilatation of the cervix is small, out of all proportion to the amount of foetal distress registered, then I am inclined to perform Caesarean section. If the dilatation is more than will admit three fingers, version is relatively simple after paralyzing the cervix with novocain one per cent. The patient is then left to deliver herself.

All are agreed that sedatives are called for in the early stage of spasm of the uterus, and this fact, coupled with the advent of sympathy which often attends their use is a further argument against the habit of labelling these patients as subjects of uterine inertia. In addition the continued use of this term conveys a totally wrong idea of the underlying clinical condition to both students and postgraduates, and it is small wonder that oxytocics are still being used to an altogether unwarranted extent.

One final remark regarding spasm of the uterus. At the start of labour the head of the child may appear to fill the cervix adequately, sympathetic activity, therefore, ought to follow according to the law I have stated. In answer to this I would say that normal uterine activity is to be expected and encouraged, but three upsetting elements may be looked out for. First a dystrophic type of individual, whose leanings in this direction have been of slow and gradual onset, and who can, therefore, not be rendered normal by a single injection of one or more hormonic extracts, or even by a course of such extracts; second an occipito-posterior position of the child, and third a large infant whose flexibility and, therefore, adaptability to the birth canal are of a low order.

The second anomaly I wish to consider is active retention of the foetus. The condition has one feature in common with uterine failure, namely that active retention is also met with in the second stage of labour. For this reason confusion in diagnosis is prone to occur at a time when accuracy is all important. The mutual characters which enable a differential diagnosis to be made with confidence are as follows:

Uterine Failure.	Active Retention of Foetus.
Presenting part shows at vulva and depresses perineum.	Presenting part depresses pelvic floor with each contraction of the uterus, receding in intervals.
Foetal or maternal distress imminent or present.	Foetal and maternal distress absent at first.
Moderate tenseness of uterus.	Uterus slack.
Second stage has lasted upwards of four hours.	Uterus slack.
Delivery with the forceps easy.	Delivery with the forceps difficult in proportion to the depth of anaesthesia, and relaxation of pelvic floor obtainable.
Uterine contractions feeble.	Contractions vary in intensity but are never strong, nor associated marked efforts to bear down.
Administration of oxytocic drugs occasionally successful. They should never be given, except in a case of gonorrhoeal discharge when the use of the forceps entails an added risk	Oxytocics will render active retention a condition of urgency, and may lead to the manual discovery of the ring of contraction. Failure to deliver with the forceps is possible, and there is a danger of rupture.

The interpretation of the development of active retention of the foetus seems to reside in the prolongation of the period of quiescence which normally intervenes between the end of the first stage of labour and the resumption of second stage contractions. If this quiescent interval is longer than four hours, the cervix is enabled to regain its tone and its thickness, finally closing round the neck and shoulders of the child. The condition is "silent" at first, anaesthesia overcomes it, and together with uterine failure the two conditions are spoken of as second-stage delay, or late primary inertia if the labour happens to have been long. The essential fact does remain that it requires only an oxytocic drug to induce the textbook characters of active retention.

In this short paper I have not made any reference to uterine inertia *per se*. I believe that our ideas on this subject have undergone, if they are not still undergoing, a most salutary revision.

If the uterus ceases to act there is usually a reason, either because it has failed to expel the child, or because obstruction has occurred.[4] In this latter instance inertia is protective in character, seeing that the only alternative must be a catastrophe.

The question then is whether sympathy of action is present in each case. If not, then it may be enlisted by administration of a sedative, or one of the simple measures daily employed.

If sympathetic action be present, the labour will be slow, medium or precipitate, and the successful issue will never be in doubt.

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Hydramnios.

BY

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OUR present knowledge as to the formation of the liquor amnii, and of the possible causes of hydramnios is almost *nil*.

I have been investigating this problem and so far have nothing to add, but I have found a method of treatment which I think is sufficiently interesting to record.

The obvious explanation of hydramnios is that it is due either to (1) excessive secretion, or (2) deficient absorption. With the idea of ascertaining if liquor amnii was absorbed into the mother's system, I decided to inject some substance into the liquor which could be traced if it was absorbed by the mother. Before doing this I thought it would be as well to see if there were any difficulties, or dangers, attending the operation of paracentesis uteri. For this purpose I chose two cases of hydramnios.

CASE I. Mrs. E. F., admitted to Queen Mary's Hospital for the East End on February 6th, 1929, about 34 weeks pregnant. The skin of the abdomen was painted with iodine and an area was chosen where there was marked fluctuation and foetal parts could not be palpated. A spinal trocar and cannula was inserted through the abdominal wall and subjacent uterine wall, an aspirating syringe was attached to the cannula by rubber tubing and 12 ounces of liquor amnii were withdrawn. A week later, on February 13th, the operation was repeated and 18 ounces withdrawn, and on March 8th a third paracentesis was performed and 21 ounces withdrawn. The patient went into labour on March 21st, at estimated term, and a normal baby, weighing six pounds two ounces, was born alive.

CASE II. Mrs. A. T., admitted to the same hospital on May 18th, 1929, about 34 weeks pregnant. Paracentesis uteri was performed on May 18th, and 42 ounces withdrawn. Labour started

on May 29th, nine days after the paracentesis, and an anencephalic foetus was stillborn, weighing four pounds.

Having satisfied myself that there was no grave danger attending the operation of paracentesis uteri, I proceeded with my investigation of the source and destination of the liquor amnii. In this I have failed completely, and I can dismiss this part of the report in a very few words. I tried injecting indigo-carmine into the liquor amnii in the hope of detecting it in the mother's urine. I tried in two cases, first with five cubic centimetres and then with ten. We could not detect a trace in the mother or foetus in either case.

Searching for something more sensitive, Professor Dodds, of the Courtauld Institute of Biochemistry, suggested insulin. We estimated the blood sugar at hourly intervals and then injected insulin. There was not any effect whatsoever. Two days later the patient went into labour, at term, and a live baby was born. We investigated another case. The only result was a very slight, almost negligible, change in the mother's blood-sugar—the wrong way! This patient was delivered about a week later of a normal living baby.

To continue my records of cases of hydramnios:

Case III. Mrs. J. I., admitted to Queen Mary's Hospital for the East End on May 23rd, 1930, with hydramnios. Forty-one ounces were withdrawn. The liquor amnii did not again accumulate, and the patient went into labour on July 28th, 1930, nine and a half weeks later, and was delivered of a living baby weighing six pounds eight ounces at term.

Case IV. Mrs. A. D., admitted to Queen Charlotte's Hospital on November 5th, 1930, 38 weeks pregnant, suffering from hydramnios. The first two attempts only produced blood-stained serum, but at the third attempt 30 ounces of liquor amnii were withdrawn. Five days later, on November 10th, 1930, I tried again, and drew off 21 ounces of liquor amnii. On November 15th, 1930, the patient went into labour. Twins were born. The first twin to present was a breech with extended legs, and was born dead, weighing five pounds one and a half ounces. The position of the second child was that of a left occipito-anterior; it was born alive, weighing seven pounds eight ounces. Evidence of placental injury was absent in both cases.

Case V. Mrs. A. C., admitted to Queen Charlotte's Hospital, 37 weeks pregnant, suffering from hydramnios. An X-ray examination disclosed one foetus. The patient had oedema of ankles (October 27th, 1931). Forty ounces of liquor amnii were

drawn off on November 3rd, 1931, and 40 ounces more on November 7th. The patient went into labour, and was delivered next day of a living baby weighing nine pounds. The baby was slightly asphyxiated. Delivery with the forceps resulted in a left facial palsy and superficial abrasion, but otherwise the child was normal and progressed well. The mother had slight pyrexia during the first five days.

CASE VI. Mrs. C. I., admitted to Queen Charlotte's Hospital on December 19th, 1931, 35 weeks pregnant, with albuminuria and oedema. An X-ray examination disclosed two foetûs. The patient was suffering from very marked hydramnios. The uterus was tapped by my colleague, Mr. Bourne, and five and three-quarter pints of liquor amnii were withdrawn. The patient went into labour soon after. Both babies presented by the breech and had extended legs and arms. The first was stillborn but did not show any signs of injury; weight: seven pounds nine ounces. The second was born in white asphyxia but soon recovered—weight: seven pounds eight ounces. The puerperium was normal.

CASE VII. Mrs. E. J., admitted to Middlesex Hospital, 25 weeks pregnant, suffering from marked hydramnios. An X-ray examination disclosed only one foetus. There was great excess of liquor amnii. The uterus was tapped in two places; 36 ounces were drawn off the first time, and 53 ounces the second time; total, 89 ounces of liquor amnii drawn off. Fourteen weeks later hydramnios, as such, was absent; the labour was normal. Twins were born. The first was stillborn and weighed three pounds ten and a half ounces; the second was alive and weighed five pounds five ounces. The puerperium was normal.

CASE VIII. Mrs. A. G., admitted to Queen Charlotte's Hospital on March 18th, 1932. She was 25 weeks pregnant and the uterus was very large. An X-ray examination disclosed one foetus only. On March 19th, 1932, the uterus was tapped in two places, two and a half pints of liquor amnii being drawn off from the first, and three and a half pints from the second, a total of six pints. On April 19th, 1932, there was not any hydramnios. On April 27th, 1932, spontaneous premature labour occurred at about the thirtieth week. Twins were born; both children being stillborn.

CASE IX. Mrs. L. H., admitted to Queen Charlotte's Hospital on October 26th, 1932. The patient was 34 weeks pregnant. An X-ray examination disclosed twins, and there was marked hydramnios. The uterus was tapped in two places, 25 ounces being drawn off the first time, and 55 ounces the second, a total

of 80 ounces. On November 8th, 1932, the amount of liquor amnii had not increased. On December 17th, 1932, twin girls were born, weighing five and a half pounds and five pounds, both alive, nearly eight weeks after paracentesis.

Case X. Mrs. H. S., admitted to Queen Charlotte's Hospital on November 30th, 1932. An X-ray examination disclosed one foetus. The patient was suffering from hydramnios, and four and a half pints of liquor amnii were withdrawn. On January 11th, 1932, the liquor amnii had not increased. On January 19th, 1932, normal labour occurred; the baby was alive and weighed eight pounds.

Cases III, VII, IX and X, demonstrate that tapping the uterus is a rational method of treating hydramnios, since all four cases were sufficently acute to demand interference, and any other line of treatment would have resulted in a very premature, and barely viable child. There do not appear to be any risks, other than the patient going into labour.

In Case IV, I apparently struck the placenta, as even when the cannula was pushed in up to the hilt blood only was withdrawn. There is not any evidence that this is in any way responsible for the death of one of the twins.

Several times I have noticed very violent foetal movements during the course of the operation, suggesting that the foetus has come up against the sharp end of the cannula.

When withdrawing more than two pints of liquor amnii it is usually necessary to re-insert the needle as, with the lessening of the contents of the uterus, the needle leans at an acute angle to the skin.

Even in acute hydramnios, such as Case VI, the liquor amnii does not appear to be under pressure. It has to be sucked out with an aspirating syringe.

(*The discussion on this paper will be found on page* 538.)

Owing to lack of space, the following article delivered at the 9th British Congress of Obstetrics and Gynaecology, held in Birmingham, will be found in the June issue of this Journal, viz:—

"The Mechanism of Uterine Action and its Disorders," by W. Blair-Bell, M. M. Datnow and T. N. A. Jeffcoate.

The Obstetrical Signficance of Tranverse Contraction of Pelvis.

BY

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EVERY obstetrician now and again happens to see cases of parturition which perplex him by their progress. Sometimes, contrary to his expectations, labour proceeds and terminates in a normal way, and artificial aid is not needed, whereas at other times labour has to be terminated artificially, although all the conditions seemed normal—size and position of the foetus, size and shape of the pelvis, and the powers of labour. It stands to reason that he will continually seek to ascertain the causes, which have foiled his own expectations, and have led to an error in his prognosis.

He will often succed in discovering these causes, and this knowledge will enable him to encounter successfully the circumstances which, during a previous labour have misled his judgment.

In my own obstetrical clinic I was occasionally struck by cases, of which the course and progress may briefly be stated thus:

Labour occurs at term. The position of presentation and attitude of the foetus are normal, and repeated examinations show the foetus to be of normal size. The pelvis does not show any anomaly,—at any rate it is not asymmetrical, and the conjugata vera is not shortened,—on the contrary, it may even be longer than normal. Neither is the inferior strait abnormal. Parturition commences, the powers of labour are strong and efficient, nevertheless the head does not become engaged. It remains floating above the plane of the inlet, and at the most it may become lodged in the superior strait with only a small segment. Finally dilatation becomes complete, and labour has to be terminated by means of version and extraction, and sometimes an additional difficulty is encountered in delivering the

aftercoming head. In the majority of cases, however, the foetus is delivered alive.

On investigation after delivery, the foetus does not appear to be of a pathological size, neither does the conjugata vera prove to be shortened.

To the question why the head was not engaged, I could not at first find any answer, until I suspected that in these and similar cases the cause of the lack of engagement of the head could perhaps be traced to a transverse contraction of the plane of the inlet, in which case we have, therefore, to do with asymmetrical pelvis, with a normal conjugata vera, but with a transverse diameter which is less than normal.

Pelvimetry has acquainted us with various forms of pathological pelves, with a transverse contraction at the plane of the inlet. As a rule, however, such pelves also present contraction of the antero-posterior diameter, and moreover they show very obvious pathological changes. As instances I may quote: the congenital generally contracted pelvis, the coxalgic pelvis, and certain forms of pelvis with dislocation of the femur.

On the other hand rarely if any mention is made in the literature of pelves which do not present any noteworthy anatomical anomaly, which are of symmetrical structure, with all but shortened antero-posterior diameter and with as the only anomaly a contraction of the transverse diameter.

We know the Naegele pelvis, in which one wing of the sacrum is partly or totally missing; but this is a pelvis with a grave anatomical anomaly.

We are also familiar with the pelvis of Robert, which shows both wings of the sacrum incompletely developed, with the result that, while the antero-posterior diameter is normal, the pelvis is markedly contracted transversely. It is common knowledge, however, that this pelvis is of rare occurrence.

Pondering over the observations aforementioned, the question urged itself to my mind whether the occurrence of "formes frustes" of the Robert pelvis, i.e. pelves with normal antero-posterior diameters but with a moderate and inconspicuous contraction of the transverse diameter, are not of greater frequency than suspected.

To gain more insight into this problem one has to overcome the difficulty of obtaining reliable measurements of the transverse diameter of the plane of the inlet.

The development of the technique of pelvimetry has led to

the result, that at present we employ the simple and effective methods by which to measure the antero-posterior diameter of the plane of the inlet, i.e. the conjugata vera to a fair degree of certainty. We may use the fingers by measuring the conjugata diagonalis and deducing from it the length of the conjugata vera; or we may employ the instrumental method whereby the conjugata vera is measured directly by means of a pelvimeter.

As regards the method of measuring the transverse diameter of the pelvic inlet, however, we have to acknowledge the fact that the digital method, as well as mensuration by means of pelvimeters, appears to be inefficient. In practice not a single pelvimeter has proved suitable as a means of measuring this diameter and I fully agree with Whitridge Williams, who wrote in his well-known and appreciated textbook: "The transverse diameter of the superior strait cannot be measured directly in the living woman and, as a rule, for all practical purposes, it is necessary only to palpate the linea terminalis with the examining fingers, and in this way roughly estimate the outlines of the superior strait." It is true, Skutch's pelvimeter may serve to a certain extent to render possible an approximate measurement of the transverse diameter, but the use of this instrument is hampered by great difficulties, especially that of determining the extreme lateral points of the said diameter.

In order to estimate the transverse diameter of the superior strait, we have in our clinic satisfied ourselves with approximate estimations which, taken as a whole, gave us some idea of the measurement of the transverse diameter of the pelvis, and more especially of that of the superior strait. However, we were well aware of the fact that thereby we by no means obtained a true knowledge of the length of the transverse diameter.

Our procedure was as follows:

1. The accessibility—total or partial—of the linea innominata to internal palpation was determined.

2. The distantia spinarum, cristarum and intertrochanterica were measured.

3. Measurements of the distance between the spinae iliacae posteriores.

4. Measurement of the pelvic circumference.

If the above-mentioned measurements were found to fall well below the normal, and if, in addition, the lineae innominatae were found to be easily accessible to palpation throughout their whole extent, or nearly so, then the conclusion was drawn that the superior strait was contracted transversely. In the case of the

congenital generally contracted pelves, for example, these measurements could be demonstrated without difficulty.

It stands to reason that, in trying to find an answer to the question I put myself, namely, whether moderate contraction transversely of the superior strait, with a normal antero-posterior diameter is not of greater occurrence than thus far suspected, the above-mentioned method of investigation had to be regarded as of little use and reliability.

Meanwhile, however, the obstetrician can turn to pelvimetry, which enables him to learn the true extent of the various diameters of the female pelvis to a much better degree of certainty than heretofore has been possible.

The obstetrician must reckon pelvimetry by means of the Röntgen-rays as one of the most valuable acquisitions for his diagnostic work during the last 15 to 20 years.

It is well known that various methods have been devised for that purpose. I will not try to expound them, but I only wish to state that the Frenchman, Fabre, was one of the first to employ the X-rays in the mensuration of the diameter of the superior strait. For that purpose he used a rectangular metal frame, each side of the frame being marked by indentations one centimetre apart. The difficulty, however, was to place the frame in a position corresponding to that of the plane of the superior strait. In order to obviate this difficulty the technique was modified in various ways. On the German side an attempt was made to measure the conjugata vera alone by letting the rays strike the pelvis from the side. I may quote in this connexion the method of Guthmann, and I wish also to mention the work of Martius in Göttingen, who reverted to the principle of Fabre. If I am not mistaken, the method mostly employed in England is that known to me as the method of Thoms. Theoretically this method is wholly acceptable. Practically, however, I wish to state that a weak point in it is, and remains, the difficulty of placing the plane of the inlet parallel with that of the film-holder.

The ideal would, therefore, be a method by which it would no longer be necessary to fix the plane of the inlet in a certain position as regards that of the film-holder.

I believe that the Röntgen specialist of the obstetrical clinic of Amsterdam, Tenbergen, succeeded, in 1924, in finding such a method. By this method it has become possible, without the aid of frames and the like, to reproduce by means of the X-rays a drawing on paper of the superior strait of every pelvis in its true

form and size, so that a true estimate of all diameters may be read off the drawing by means of a measure.

The accuracy and reliability of this method has been tested over and over again in numerous investigations on the cadaver.

Tenbergen calls his method the redression-method. A complete description would entail an extensive physico-mathematical exposition. I wish to refrain from such, especially as I am capable of doing so, only to a slight extent.

As regards the principle, however, I wish to give you a short description.

From two points, situated in the sagittal plane above the pelvic inlet, and at a distance of 15 centimetres from each other, two Röntgen photographs of the pelvic inlet are taken.

In a manner which corresponds in principle with the method adopted in determining the exact locality of corpora aliena in the body, it is possible to determine by means of these two Röntgenograms the exact position of the plane of the pelvic inlet, as regards first the position of the Röntgen tube and next that of the photographic plate. If this is known, it is possible to obtain photographically from one of the Röntgenograms the natural size of the pelvic inlet.

For this purpose the Röntgenogram is placed in front of the camera in the same position as regards the objective as that in which the photographic plate stood as regards the focus of the Röntgen rays when the Röntgenogram was made, and the ground-glass plate of the camera is so placed that it stands at an equal distance and under the same angle with regard to the subjective as the plane of the pelvic inlet stood with regard to the focus of the Röntgen tube. In this way, as can be determined by mathematical calculations, an image of the natural shape and size of the pelvic inlet can be obtained on the ground-glass plate. This image can then be photographed or traced.

For the practical application of this method, named the redression-method, a simple apparatus was constructed by means of which the Röntgenologie, mensurations of the pelvic inlet can be performed in a minimum of time in our clinic.

I refrain from considering in detail the fundamentals of this method since this would entail a lengthy, dreary physico-mathematical exposition. Willingly, however, I offer to have it described fully in one of the English obstetric journals.

It is a rule at my own clinic that all cases in which the digital and instrumental methods of examination point to anomalies

of the pelvis, and more particularly of the superior strait, are subjected to a new X-ray mensuration according to the method of Tenbergen. The drawing obtained by this method, representing the natural size of the superior strait, is assigned a place in the case-papers of the patient.

In order to gain an insight into these cases in which, notwithstanding a normal conjugata vera, without any asymmetry of the pelvis, with normal size of the foetus and with efficient powers of labour, the head experiences difficulty in becoming engaged, I have, in conjunction with my assistant, Dr. de Vries, carefully selected 43 of these cases. All those cases were eliminated in which it was found, or conjectured, that some cause was responsible for the abnormality.

In all these cases:

1. Labour had lasted 40 hours or more, the powers having been efficient.
2. The head was not engaged.
3. Labour had to be terminated artificially.
4. The conjugata vera measured 11 centimetres or more.
5. The weight of the foetus was less than 4,000 grammes.

By selection, therefore, I have collected 43 cases in which there was no obvious explanation to be given for the arrest of the progress of labour at the superior strait.

Of all these cases I had the superior strait determined according to the X-ray method of Tenbergen. This investigation revealed the noteworthy fact that in 20 out of 43 cases, i.e. in 44 per cent, with a normal or even greater conjugata vera, there existed a contracted transverse diameter. The contraction amounted to at least 1.5 centimetres. The normal for the conjugata transversa was taken as 13.5 centimetres.

Having completed the investigation of this series of cases, subsequently similar cases in the clinic have been subjected to the same method of examination. The results have more often than not verified the previous findings.

The fact could, therefore, be established that contraction of the transverse diameter at the plane of the inlet, with a normal antero-posterior diameter, was of more frequent occurrence than heretofore had been suspected.

What then was the true nature of these pelves? The Röntgen photographs showed the general development of these pelves to be more or less normal, i.e., there was not any abnormality of growth, or development.

We have also paid special attention to the development of the sacrum. It became obvious, however, that it was not so easy as it was at first surmized to gain information from X-ray photographs as regards developmental anomalies of the sacrum. Nevertheless, in some cases it appeared, without doubt, that the wings of the sacrum were hypoplastic on both sides. This fact inclines us to adopt the view that these transversely contracted pelves, with normal antero-posterior diameters are "formes frustes" of the well-known pelvis of Robert. Whether this disturbance in the process of growth has to be attributed to congenital defective centres of ossification, or to osteoarthritis acting on the iliosacral joints, is still an open question as regards the pelvis of Naegele and that of Robert, and even more so for the anomaly of the pelvis to which I have here tried to direct your attention.

Summarizing, I think the following three conclusions are justified:

1. In cases of labour in which the antero-posterior diameter of the superior strait is normal and yet the engagement of the normal foetal head does not occur, while there is no apparent reason for such lack of engagement, one should think of the possibility of a contraction of the transverse diameter of the superior strait.

2. Pelves showing only this anomaly are of greater occurrence than heretofore suspected.

3. The diagnosis of this anomaly of the pelvis can be made only with the help of mensuration by means of the X-rays, whereby the true shape and size of the superior strait, in its entirety, can be determined accurately.

In the eighteenth century a Dutchman and an Englishman, van Deventer and Smellie, laid the foundations of pelvimetry in so far as it was of special significance for obstetrics. To compare our work with the standard investigation performed by these two talented workers would indeed imply impudence. Nevertheless, I trust that I may appeal to my English colleagues to pay due attention in their practice and in their clinics, to the subject which I have had the honour of bringing to your notice.

(*The Discussion on this Paper will be found on page* 538.)

Discussions on Papers.

DISCUSSION ON PROFESSOR OSKAR FRANKL'S PAPER.

In opening the discussion on Professor Frankl's paper, Professor Dougal (Manchester) said: That I am the first to speak in the discussion on Professor Frankl's paper does not mean that I have any special knowledge of the isthmus uteri, far from it, but rather that I am anxious not to lose any time in expressing our appreciation of a most interesting and instructive piece of work.

Professor Frankl has presented his thesis so thoroughly and with such a wealth of beautiful illustration that I am not surprised to learn that the work has taken more than five years to complete, and I think you will agree with me that he is paying our Congress a very great compliment by coming here to-day and allowing us to be the first to hear the results of his investigation.

As I understand it, the isthmus uteri is a pars intermedia between the body of the uterus and the cervix—a sort of no man's land belonging definitely neither to one nor to the other. The endometrium resembles that of the body of the uterus, but its response to hormonic and pathological stimuli is smaller or absent and the glands have a tendency to become cystic. During pregnancy the isthmus belongs more to the body of the uterus, taking part in the general hypertrophy, forming a decidua, though in a modified form, and providing the lower part of the cavity which houses the ovum. During labour, however, the isthmus definitely sides with the cervix, and as the lower uterine segment its role is purely a passive one. Indeed its existence during labour is uneventful so long as the action of the powerful upper segment is not seriously challenged. If it is, then the isthmus becomes a sort of obstetrical cockpit and is apt to be weakened or seriously damaged amidst the clash of the contending forces. That has been my conception of the isthmus uteri, but after hearing Professor Frankl this morning I realize that there is a good deal more in the subject and that we shall have to take account of the isthmus in the study of a number of other obstetrical and gynaecological problems.

Yesterday our mental processes were subjected to a strain from which some of us have not yet fully recovered, and it is probable that Professor Frankl's paper contains much more than we can comfortably assimilate in the short time at our disposal this morning; but we look forward to seeing it printed in full in our Journal, when we shall be able to realize even more than we do to-day its importance as a contribution to obstetrical and gynaecological anatomy, physiology, and pathology.

Professor BLAIR-BELL (Liverpool) congratulated Professor Frankl on his excellent demonstration, which he thought had well repaid, in its scientific excellence and completeness, the labour expended upon it. He also paid a tribute to Professor Dougal for the admirable manner in which he had opened the discussion.

For himself, he felt that a flood of light had been thrown on many of the

problems of the lower uterine segment, or isthmus. What Professor Frankl had said about the deposition of glycogen and also of the implantation of the placenta was very interesting.

Professor Blair-Bell reminded those present of the work of Professor Chipman, of Montreal, published in the Laboratory Reports of the Royal College of Physicans, Edinburgh, in 1903, concerning placentation in the rabbit, and the distribution of glycogen in the maternal decidua, first described by Claude Bernard in the pregnant uterus in 1859. He had himself recently discussed this subject (*Journ. Obstet. and Gynaecol. Brit. Emp.*, 1928, xxxv, 233). Professor Blair-Bell called attention to the so-called "uterine milk" which was absorbed by the apposed placenta of the ungulates from which processes dipped down between cotyledous and into the maternal glands, and absorbed nutriment from the maternal tissues.

Professor Blair-Bell further asked Professor Frankl whether in his work he had obtained any information of interest regarding the development of the lower uterine segment, the cervix, uterus and vagina, concerning which new work had recently been done. He thought that the fact that the musculature of the whole uterus and vagina was formed in a continuous sheet of mesoderm was evidence in favour of combined origin. That the lower uterine segment, as the vagina, was supplied with blood from a separate branch, or from special branches, of the uterine artery appeared to him to have some developmental significance, and he would greatly value Professor Frankl's views on the subject.

Dr. NINIAN FALKINER (Dublin) raised the question of the ultimate value of glycogen as a means of nutriment to the ovum prior to embedding. He stated that the period between the arrival of the ovum in the uterus and the commencement of embedding was very short, that the glands had open mouths leading directly into the uterine cavity, and suggested that some resorption of glycogen took place—resulting in the temporary storage of glycogen in the stroma cells of the stratum compactum. In this way, he argued, the metabolism of glycogen by the ovum could be more easily explained.

Dr. Falkiner added as his reason for this contention that placentation in the case of the human ovum came into the type of "haemo-chorialis."

In reply to the discussion Professor O. FRANKL (Vienna) said: I am extremely grateful to all gentlemen who were good enough to speak in this discussion. As far as it concerns the glycogen and its significance for the nutrition of the ovum in early stages after implantation, I agree with the speaker who said that if the glycogen is only in the epithelium and in the lumen of the glands it would be eliminated without being of any service to the ovum. But the glycogen may be found also in the connective tissue around the glands, and here the ovum implants. Not only does glycogen fertilize the mucosa but the oedema fluid is of significance here also. Oedema is not simply water, but also contains large amounts of protein. Therefore in the body of the uterus the mucosa is always oedematous at the end of the pre-menstrual (pre-gravid) stage.

Concerning the question of implantation of the ovum I will give you—thanks to the fine work of Grosser—some schemata of comparative descrip-

tion. The nutrition of the human ovum is haemo-chorial. This is the end of gradual evolution we see in animals, being represented by the following types. If the villi dip down into the glands the foetal epithelioma is in touch with the glandular epithelium, Grosser speaks about epithelio-chorial type. In other animals the glandular epithelium is destroyed and the foetal epithelium gets contact with the maternal connective tissue—this is the syndesmo-chorial type. In the next group of animals we speak about endothelio-chorial type, as the villi touch maternal vessels. The human ovum opens maternal vessels, the foetal epithelium is in most intimate touch with the maternal blood—this is the haemo-chorial type. Before the vessels are opened the ovum also in the human uterus ought to be nourished by something, and at this stage also in human beings we have to speak about syndesmo-chorial type of nutrition.

Concerning development of the isthmus it has to be said that we must modify our old opinions according to the present research of Dr. Vilas, who showed that the vagina does not develop from the Müllerian ducts.

DISCUSSION ON Mr. ALECK BOURNE'S PAPER.

Dr. G. Dick Read (Woking) said: There is one sub-heading in Mr. Aleck Bourne's paper which I should like to lay stress on, and that is the importance of prophylaxis of fear during pregnancy.

Very few women of the cultured races go through labour without some moments of apprehension or even fear, and the large majority of women, either from education or from instinct, are possessed of anxiety or fear from the earliest stages of labour, and it is not unnatural, since the agonizing pains of labour are usually communicated with some zest by friends or relations to the expectant mother. She reads of its torments in the Bible, and the Prayer Book refers to its pains and dangers.

Fear is an instinct essential for the protection of the species against the dangers which may destroy the individual, and its emotional stimulus produces physical results through the sympathetic nervous system.

The mechanism of evacuation depends upon the neuro-muscular harmony, the inhibitory nerves supplying the circular muscles act in opposition to the motor nerves of the longitudinal muscle fibres. The stimulus to evacute not only produces expulsive longitudinal contractions of the muscles of the viscus, but also, in opposition to the nerve-supply of the constrictor muscles, causes relaxation of the circular fibres. Examples of the effect of fear or pain, which to a large extent are synonymous, are seen in the inhibition of defaecation in a constipated baby and the retention of urine in cases of acute urethritis.

There is very little doubt that emotional stimulus reaches the uterus through the sympathetic nervous system, and whether or not uterine contractions are influenced by the lumbo-sacral autonomic system when fear is pronounced, the sympathetic nerves supplying the circular fibres of the uterus override the influence of whatever nervous stimulus is motor to the longitudinal fibres.

Since the circular fibres are almost entirely confined to the body, lower segment and cervix of the uterus, they exert, when contracting, very definite

resistance to expulsive efforts, and instead of an easily dilating cervix there is resistance to each expulsive effort of the longitudinal fibres.

It is well known to clinicians that the nervous patient is the slow dilator, and there is evidence which strongly suggests that the nervous patient actually resists, through the stimulus of fear, the dilatation of the birth canal. As the uterus contracts more powerfully to expel under influences which are probably not nervous in origin, so in time the resistance of the cervix and lower uterine segment to the oncoming foetal head is broken down, but not before many of the complications of prolonged labour have resulted.

Fear is the fundamental cause of a large number of cases of uterine inertia. It has been gratifying to see the change which comes over some cases of labour when fear, by means other than anaesthesia, has been allayed.

Such an abnormal strain placed from the earliest stages of labour upon the longitudinal muscles must have a marked effect upon the conduct of labour. This strain causes pain, and pain increases fear, and fear in turn supplies the stimulus to fresh resistance, and it is within this vicious circle that the secret of a large number of slow labours exists.

May I, before stopping, touch lightly upon the question of treatment. By the use of the practised art of scientific relaxation labour becomes, in a great many cases, almost dramatically simple, and without illustrating by examples, or in any way calling upon your credence, I would say that there is not any greater prophylaxis to uterine inertia than the conducting of labour with the woman in a complete state of relaxation which has previously been taught and practised.

There appears little doubt that at least one of the prevalent causes of long, painful and exhausting uterine contractions can be eliminated by combating the abnormal emotional stimulus which culture has inflicted upon the women of to-day.

Mr. RIVETT (London) said that in uterine inertia some abnormality of the endocrine secretion and rigidity of the cervix played important parts. When performing Caesarean section he had noticed differences in the thickness of the uterine muscle. Abnormal musculature might well be the cause of irregularities in uterine action. A case was described in which he had made multiple incisions, about a quarter of an inch in length, into the cervix and had thus facilitated labour. In another patient the cervix was dilated to the size of a half-crown; he applied the forceps through the small cervix and tied the handles together and attached a weight to them; delivery occurred 23 hours later. Two other cases were mentioned in which he had employed multiple incisions of the cervix. He asked if there were any means of diagnosing such cases early in labour and also what was the best line of treatment to be adopted.

DISCUSSION ON MR. A. A. DAVIS'S PAPER.

Mr. FRANK COOK (London) congratulated Mr. Davis on his admirable exposition, but challenged him to adduce experimental or pharmacological evidence to prove the existence of that para-sympathetic nerve supply to the uterus which he had assumed on anatomical grounds. Professor Beckwith Whitehouse would agree that his published clinical observations in this direction were suggestive rather than confirmatory.

Mr. W. C. W. NIXON (London) asked whether the specimens of the presacral nerve had been removed for the condition of spasmodic dysmenorrhoea. He referred to Cotte's publication, in which it was stated that in some of the cases of pelvic sympathectomy, pregnancy had supervened and labour had been normal. He was interested to hear of the finding of a sub-epithelial layer of nervous tissue in the infra-vaginal portion of the cervix, for during the course of histological examination of normal cervices he had been impressed by the constant presence of a fine layer of elastic tissue in the same region. He had used Sheridan's elastic stain to demonstrate this.

DISCUSSION ON FAHMY'S PAPER.

O. FRANKL (Vienna) said: The problem on post-menopausal bleeding is most interesting and stands in the very centre of discussion at present also in the German literature. Of course it is easy to explain such haemorrhages in cases of uterine cancer, uterine polypi, and myomata. In cases of ovarian tumours the development of haemorrhage may be easily understood in some instances, but not so in others. Granulosa-cell tumours are most interesting in this respect, about which Schiffman was the first to publish a paper concerning post-climacteric haemorrhages. These tumours are of general significance far beyond our more narrow field of gynaecology, for these are tumours which positively exert an hormonal action. We have learned in our schools that tumour-cells do not function normally. In general this holds here; but tumours originating from endocrines take here a special position. We know, for instance, by the observation of von Eiselsberg, that thyroid cancer may provoke hyperthyroidsm, resection may produce hypothyroidism, and metastasis may again provoke disappearance of symptoms. Also the cells of granulosa-cell tumours exert an endocrine action. These cells do not only look like granulosa cells but act in the same way. They produce folliculin. As this hormone is produced in abundance without any existence of luteo-hormone, we see the same effects in haemorrhagic metropathia—hyperplasia of the myometrium and endometrium—bleeding. Far more difficult is the explanation of bleeding in cases of ovarian fibromata. I saw a case in a woman aged 53 which was connected with hyperplasia of the myometrium and of the mucosa and severe bleeding. Hormonal action may be excluded there. Whether congestion due to mechanical factors is to be held responsible cannot be decided so far.

DISCUSSION ON LLOYD'S AND GANNER'S PAPER.

O. FRANKL (Vienna) said: I remember a case of fundal rupture which was similar to the reported case of Mr. Ganner. But in our case it was easier to find the aetiology, because the Fallopian tube and the tubal insertion into the uterus had been previously excised. The examination of the edges next to the rupture did not show any fibrosis; but I saw that the decidua had grown far deeper down than expected. Evidently there had existed a deep depression, a sort of diverticulum, as the union of musculature after the excision was an incomplete one. And this case reminds me of another case, reported by Schante a long time ago, which I had also examined.

After a cervical Caesarean section the uterus was removed some years later. Here one saw the cervical mucosa growing deep into the cervix musculature, also producing something like a diverticle, due to incomplete union of the musculature of the cervix. I think that after a currettment which has been performed too energetically such diverticles may originate, the wall of the uterus becomes less resistant, and the rupture may start here. In cases of uterine rupture at the usual place I have never seen any fibrosis.

DISCUSSION ON MR. L. CARNAC RIVETT'S PAPER.

Professor HENDRY (Glasgow) congratulated Mr. Rivett on his success with paracentesis in the treatment of cases of hydramnios. This method had been tried by Wormser in 1912, and again by Henckel in 1919, but the results were unsatisfactory; Seitz condemned the procedure as "useless, and not without danger." The treatment of hydramnios is bound up with the prognosis for the foetus; the danger to the mother is seldom great. The frequency of the association of foetal deformity with hydramnios has been variously recorded from about 10 per cent to almost 40 per cent, but in only one of Mr. Rivett's cases was this present.

With a view to assessing the prognosis for the foetus in all cases of hydramnios, Krahula, in 1921, collected records of 154 cases from the Frauenklinik and the Poliklinik in Bonn, and of other 157 published cases—there were 151 single children, 64 pairs of twins, and three cases of triplets. Of the 291 children 103 were stillborn, 76 died soon after birth, and only 11 were recorded as having survived in good health: in 17 cases the children were recorded as being born alive, but without any note as to survival, and in 84 there was not any record as to the condition at birth or the survival of the child. From this series Krahula gives the distressingly low figure for healthy survival as less than four per cent. He accepts for this purpose only the 11 cases in which an accurate record was available. Mr. Rivett's figures are most encouraging in that there were 12 liveborn children out of the 16 in the series.

It is certainly essential that before this treatment is carried out the patient should be X-rayed with a view to detecting any gross foetal deformity which might make this conservative form of treatment futile.

Mr. RIVETT (London), in reply, said that he had not followed up the histories of the infants since they had been born. He did not see any difficulty in doing so and he would endeavour to get in touch with the families concerned. In his series of cases he had neither observed that any injury had occurred to the foetus nor had any complication been noted owing to the placenta being transfixed by the needle.

DISCUSSION ON PROFESSOR VAN ROOY'S PAPER.

Professor DOUGAL (Manchester) said: There are two points which have specially interested me in Professor Van Rooy's paper. The first is the frequency of transverse contraction of the brim of the pelvis. A good deal has been written in recent years about transverse contraction of the outlet,

possibly rather more than the subject deserves, and it is extremely interesting to find that a similar contraction at the brim is not nearly such a rarity as was formerly supposed.

The second point concerns the diagnosis of these contractions by radiological methods. With one or two notable exceptions this form of pelvimetry has been almost completely neglected in this country, and I think it is time that we revised our estimates of its value. I understand from what various radiologists have told me that radiopelvimetry is just as accurate as our older clinical methods, and it is high time that we gave it a thorough trial. The trouble is that most of our maternity hospitals are not equipped with the proper apparatus; but we should insist on such being provided, because there is already a very great field for radiological work in obstetrics. I refer to the diagnosis of malpositions, foetal abnormalities, maturity, and so on. The addition of radiopelvimetry would so enlarge that field that the provision of proper apparatus in every up-to-date maternity hospital would become urgent.

Mrs. ADAMSON (Leeds) said that she had had some experience of X-ray examination during pregnancy for two reasons: (1) that she worked in Leeds, where contracted pelvis cases were frequent, and (2) that Dr. Leo Rowden, a pioneer in this work, practised there and was readily available. Dr. Rowden can obtain exact measurements of the pelvic inlet by placing the patient in a reclining position, and his findings are of great help when external measurements would lead one to suspect contraction of the true pelvis.

Even when pelvic contraction was known to be present she considered "trial labour" valuable and justified in its results.

Professor VAN ROOY, in reply, said: The investigations about the cause of the transverse contraction are not yet ended. I believe, however, that the wings of the sacrum are congenitally atrophied in the cases I studied.

I am convinced that the more X-ray mensurations of the whole inlet of the pelvis will be made, the more anomalies, till now unknown, will be found.

As to therapy, in cases with a low transverse contraction I induced premature labour; in cases with a transverse contraction of about three centimetres or more I terminated pregnancy by Caesarean section.

My aim has been to awake attention for this anomaly of the pelvis, about which, till now, we had but little knowledge.